

Treatment with anti-cancer drug T-DM1 after pertuzumab is 'good option'

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Patients with HER2-positive breast cancer, whose disease has progressed after being treated initially with pertuzumab in combination with trastuzumab and a taxane, can respond well to treatment with T-DM1—a drug that combines trastuzumab with an anti-cancer drug called DM1.

Dr. Benedetta Conte, a medical oncology resident from the University of Genova, Italy, told the Advanced Breast Cancer Fifth International Consensus Conference (ABC5) in Lisbon today (Friday) that, until now, there was little evidence for the efficacy of T-DM1 as a second-line treatment in patients who had received pertuzumab as part of their first line of therapy, and whose breast [cancer](#) had started to spread to other parts of the body (metastasise).

However, findings from the largest group of patients to be treated this way and in a real-world setting (as opposed to a randomised clinical trial) showed that T-DM1 treatment resulted in the cancer shrinking or disappearing in a third of patients (an objective response) and nearly 40% of patients continued on the treatment for at least six months with their disease under control.

The study is published in *Clinical Breast Cancer* journal today.

Dr. Conte said: "Our study showed T-DM1 had a meaningful clinical effect after first-line pertuzumab. The length of time that patients lived on T-DM1 treatment without their disease getting worse was an average of over six months. The results from our study are real-world data,

which improve the available evidence for recommendations for treatment of metastatic breast cancer after it has failed to respond or has returned after initial therapy, and show that T-DM1 is a good option for these patients."

Dr. Conte and her colleagues identified 77 out of 2034 patients who were enrolled in the multi-centre, Gruppo Italiano Mammella (GIM) 14/BIOMETA study looking at treatment patterns and outcomes in patients with metastatic breast cancer. The 77 patients had metastatic, HER2-positive breast cancer and had received second-line treatment with T-DM1 between November 2013 and May 2018 after initial treatment with pertuzumab, trastuzumab and a taxane. The study had a prospective part (patients diagnosed with metastatic breast cancer after the beginning of the study in April 2016 and whose data were collected prospectively), and a retrospective part (patients diagnosed from January 2000 to March 2016).

After an average (median) follow-up of seven months, the median progression-free survival was 6.3 months and time to treatment failure was seven months. Nearly 40% of patients (37.6%, 29 patients) experienced prolonged control of their disease for at least six months, with an objective response rate of 27%. By April 2016, the overall survival rate one year after T-DM1 treatment began was 82%. When the disease progressed, metastases occurred or increased in the [central nervous system](#) (CNS) in 18 patients (23%), of whom 13 already had CNS metastases at the start of the study.

The reason why there has been so little evidence of the efficacy of T-DM1 after initial treatment with pertuzumab, trastuzumab and a taxane is because a previous trial, EMILIA, reported in 2012 that T-DM1 after initial treatment with trastuzumab and a taxane was better than lapatinib plus capecitabine; progression-free survival was 9.6 months, with an objective response rate of 44%. However, it did not investigate T-DM1

after initial treatment with pertuzumab in combination with trastuzumab and a taxane since, at the time the study was made, this combination was not yet the standard of care. As a result of EMILIA, T-DM1 was approved as a second-line treatment before data on the efficacy of pertuzumab became available. When the pertuzumab data did become available, pertuzumab combined with trastuzumab and a taxane became the standard first-line therapy. But T-DM1 continued to be used as the standard second-line treatment without much evidence of its efficacy after the use of pertuzumab.

Dr. Conte said: "We can draw the following conclusions from our study: 1) compared to results from the EMILIA trial, T-DM1 shows a decreased efficacy in real-world patients receiving first-line pertuzumab; 2) although its efficacy is reduced in pertuzumab-resistant disease, T-DM1 is still associated with a clinically significant response rate and disease control; 3) although the previous exposure to pertuzumab is likely to be the main reason explaining the difference of T-DM1 efficacy between our study population and women enrolled in the EMILIA trial, there are other factors that might have partially accounted for the difference in progression-free survival. Perhaps the most important was the higher incidence of central nervous system metastases in our study population. Indeed, the progression-free survival we observed in our study is similar to that of patients with central nervous system metastases enrolled in the EMILIA trial."

As it is common for advanced breast cancer to metastasise to CNS sites such as the brain, evidence from the real world of how these patients respond to T-DM1 is important.

"Progression of central nervous system lesions was the reason for T-DM1 discontinuation in a greater proportion of patients in our study," said Dr. Conte. "These data underline the need to include patients with central nervous system metastases in randomised controlled trials. These

patients are a significant proportion of HER2-positive metastatic [breast cancer](#) patients in the 'real-world', and they are likely to respond differently to anti-HER2 agents compared to women whose disease does not involve the central nervous system."

Chair of the conference, Professor Fatima Cardoso, Director of the Breast Unit of the Champalimaud Clinical Centre in Lisbon, Portugal, who was not involved with the research, said: "This study contributes to answering an important question for which we lacked higher evidence: is T-DM1 efficacious in patients after their disease has progressed following initial treatment with [pertuzumab](#), trastuzumab and a taxane—the combination that is now the standard first-line treatment for HER2-positive [breast cancer](#)? These results suggest that for 30-40% of patients, T-DM1 can make an important difference. The result that 82% of patients were alive after one year is impressive and proves once again the importance of continuing to treat these patients with anti-HER2 therapies. When we are not able to do so, the disease progresses faster and death occurs much quicker. In several countries oncologists are only allowed to provide one line of anti-HER2 therapy and this has severe consequences for patients. This study provides more evidence that anti-HER2 therapies prolong the lives of patients and should be made available to them."

More information: Abstract no: OR65, "T-DM1 efficacy and activity in HER2-positive metastatic breast cancer patients progressing after frontline taxane plus pertuzumab and trastuzumab: an Italian multicentre observational study of the Gruppo Italiano Mammella (GIM) study group", by Benedetta Conte, 09.40 hrs GMT, Friday 15 November, Best Abstracts session.

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