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## **Combining Atezolizumab with Neoadjuvant Chemotherapy Does Not Improve Pathologic Complete Response Rates for Patients with Triple-Negative Breast Cancer**

SAN ANTONIO — The addition of the anti-[PD-L1](#) immunotherapeutic atezolizumab (Tecentriq) to neoadjuvant chemotherapy for patients with [triple-negative breast cancer](#) (TNBC) did not improve the rate of [pathologic complete response](#) when compared to chemotherapy alone, according to preliminary results from the [NeoTRIPaPDL1 trial](#), which were presented at the [San Antonio Breast Cancer Symposium](#), held Dec. 10-14.

“TNBC is an aggressive subtype of breast cancer with a high probability of relapsing,” said Luca Gianni, MD, president of the Fondazione Michelangelo in Milan. “Currently, the only treatment for early-stage TNBC is chemotherapy. While chemotherapy can be successful in some patients, relapse and resistance to chemotherapy are common, even after good initial responses.”

In this study, Gianni and colleagues examined the effect of adding the [immune checkpoint inhibitor](#) atezolizumab to neoadjuvant chemotherapy. “TNBC tumors often harbor immune cells called lymphocytes,” explained Gianni. “We reasoned that treating patients with an immune checkpoint inhibitor, in combination with chemotherapy, could boost the antitumor immune response.” Atezolizumab in combination with the chemotherapy drug nab-paclitaxel is currently approved by the U.S. Food and Drug Administration and the European Medicines Agency for the treatment of some patients with locally advanced or metastatic TNBC.

The study enrolled 280 female patients, aged 18 or older, with early high-risk and locally advanced or inflammatory TNBC. Patients were randomly assigned to receive neoadjuvant carboplatin and nab-paclitaxel (Abraxane), which are both chemotherapy drugs, with or without atezolizumab. The primary aim of the study, which is ongoing, is to determine five-year event-free survival rates. The secondary aim is to determine the rate of pathologic complete response, which can be a good predictor of long-term outcomes, explained Gianni.

Gianni and colleagues reported the data on pathologic complete response. They found that the addition of atezolizumab to neoadjuvant chemotherapy for approximately six months resulted in slightly higher rates of pathologic complete response when compared to neoadjuvant chemotherapy alone in the intent-to-treat population (43.5 percent vs. 40.8 percent); however, the increase was not statistically significant. Among patients whose tumors tested positive for PD-L1, 51.9 percent of patients in the atezolizumab plus chemotherapy arm had pathologic complete responses compared to 48.0 percent of those in the chemotherapy only arm, but this difference was also not significant.

“Our observations may indicate that there is no therapeutic benefit to adding atezolizumab to neoadjuvant chemotherapy compared to chemotherapy alone, or it may simply mean that any

beneficial effects of the combination will be seen in the long term,” said Gianni. “Pathologic complete response does not provide information about the quality of response, which is why we did not use it as the primary endpoint for this study. Further analyses may reveal differences in the quality of response between the treatment groups.”

Biological samples collected from patients before, during, and after neoadjuvant treatment will be examined for lymphocyte infiltration, DNA mutations, and/or levels of [circulating tumor DNA](#), which may reveal differences between the treatment groups, added Gianni.

Gianni and colleagues also reported that atezolizumab was well tolerated in the majority of enrolled patients. Immune-mediated adverse events of any grade were observed in approximately 8 percent of patients. Infusion reactions were the most commonly observed immune-mediated adverse event, and approximately 1.4 percent of infusion reactions were grade 3 or higher.

A limitation of the study is that the reported results are limited to the initial effects of the combination treatment and do not account for the effects of therapies administered after surgery.

This study was sponsored by Roche and Celgene. Gianni has served advisory roles for ADC Therapeutics, AstraZeneca, Celgene, Eli Lilly, G1 Therapeutics, Genentech, Genomic Health, MSD, Oncolytics Biotech, Odonate Therapeutics, Onkaido Therapeutics, Roche, Pfizer, Taiho Pharmaceutical, Sandoz, Seattle Genetics, Synthron, and Zymeworks. Gianni has consulted for Forty Seven Inc., Genenta Science, METIS Precision Medicine, Novartis, Odonate Therapeutics, Revolution Medicines, Synaffix, and Zymeworks. Gianni has received support for research from Zymeworks, Daiichi Sankyo, Zymeworks, and Revolution Medicines. Gianni is a co-inventor on a patent for PD-L1 expression in anti-HER2 therapy.

#### **ABSTRACT**

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Pathologic complete response (pCR) to neoadjuvant treatment with or without atezolizumab in triple negative, early high-risk and locally advanced breast cancer. NeoTRIPaPDL1 Michelangelo randomized study

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**Background:** Triple negative breast cancers of high proliferation or grade are a subgroup characterized by very poor prognosis, rapid progression to metastatic stage and rapid onset of resistance to chemotherapy after initial response. As a whole, triple negative breast cancer (TNBC) represents a specific area of medical need, in which new therapeutic approaches deserve appropriate test. Retrospective data showed that a subset of patients have an ongoing immune

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response within the tumor microenvironment, and that PD-L1 expression is an adaptive method of tumor resistance to tumor infiltrating lymphocytes, which in turn are needed for response to chemotherapy. Overall, the data suggests a role for immune regulation of response to chemotherapy, and support the concept that blockade of immune check-points may favor the achievement of durable response by immune mechanisms themselves, and in combination with classical chemotherapy.

**Methods:** In this multicenter open label study (NCT002620280), a total of 280 patients with TNBC were randomized to neoadjuvant carboplatin AUC 2 and abraxane 125 mg/m<sup>2</sup> iv on days 1 and 8, with or without atezolizumab 1200 mg iv on day 1. Both regimens were given every 3 weeks for 8 cycles and were followed by surgery and by 4 cycles of an anthracycline regimen as per investigator choice. The primary aim of the study is to compare event-free survival 5 years after randomization of the last patient. Important secondary aim is the rate of pCR (defined as absence of invasive in breast and lymph nodes). The comparison among treatments will be carried out by a two-sided Cochran-Mantel-Haenszel test, controlling for disease stage (early high-risk vs locally advanced) and PD-L1 expression (positive vs negative). The primary population for all efficacy endpoints will be the ITT (intent-to-treat) population, the safety population is defined as all randomized patients who received at least one dose of either regimen. pCR and safety data will be presented at the meeting. Patients will continue to be followed up to allow for assessing comparative long-term event-free and overall survival analyses. Supported in part by unrestricted grants from Hoffman-La Roche, Ltd, Switzerland and Celgene International Sarl, Switzerland

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