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To interview Peter Schmid, contact Julia Gunther at julia.gunther@aacr.org or 215-446-6896. For a photo of Schmid, click [here](#).

Neoadjuvant Treatment with Pembrolizumab Improves Pathologic Complete Response Rates for Patients with Triple-Negative Breast Cancer with Lymph Node Involvement

SAN ANTONIO — The addition of the anti-[PD-1](#) immunotherapeutic pembrolizumab (Keytruda) to neoadjuvant chemotherapy increased the rates of [pathologic complete response](#) (pCR) in patients with [triple-negative breast cancer](#) (TNBC) who had lymph node involvement, according to results from the [KEYNOTE-522](#) trial, which were presented at the [San Antonio Breast Cancer Symposium](#), held Dec. 10-14.

Results on pCR rates from this trial were [previously](#) presented at the European Society of Medical Oncology annual meeting, held earlier this year. The latest data presented here included subgroup analyses of patients with lymph node involvement.

“TNBC is an aggressive subtype of breast cancer with a higher recurrence rate within the first five years after diagnosis compared to other subtypes,” said [Peter Schmid, MD, PhD](#), professor of cancer medicine at Barts Cancer Institute in London. “It has been known for some time that involvement of lymph nodes is associated with an even higher risk of recurrence in patients with TNBC.”

The current standard of care for early-stage TNBC is chemotherapy. Large analyses have demonstrated that patients who have a pCR to neoadjuvant chemotherapy have a positive outlook with very low rates of recurrence, particularly in patients with more aggressive cancers like TNBC, explained Schmid.

“Currently, the pCR rate for standard chemotherapy treatment using an [anthracycline](#) and [taxane](#) combination is about 40 percent, or about 50 percent if a platinum-based drug is added to the combination,” added Schmid. “There continues to be a significant need for new regimens that can increase the pCR rate and increase long-term, event-free survival for patients with TNBC.”

In this study, Schmid and colleagues examined the effect of adding the immune checkpoint inhibitor pembrolizumab to neoadjuvant chemotherapy and adjuvant therapy in patients with early-stage TNBC. Treatments targeting the PD-1/PD-L1 pathway were previously shown to be effective for patients with metastatic TNBC.

The study enrolled 1,174 patients, aged 18 years or older, with previously untreated, non-metastatic, centrally confirmed TNBC. Patients were randomly assigned 2:1 to receive either pembrolizumab plus chemotherapy or placebo plus chemotherapy as neoadjuvant treatment. After neoadjuvant treatment, patients underwent definitive surgery and received radiation therapy as indicated. Patients received either adjuvant pembrolizumab or placebo until

recurrence or unacceptable toxicity. The primary endpoints of the study, which is ongoing, are pCR and event-free survival.

Schmid and colleagues have previously reported that patients in the pembrolizumab plus chemotherapy arm had a significantly higher rate of pCR compared to patients in the chemotherapy alone arm (64.8 percent vs. 51.2 percent), regardless of PD-L1 expression.

The latest data presented here showed that among patients whose cancers had spread to the lymph nodes, 64.8 percent of those in the pembrolizumab plus chemotherapy arm had a pCR, compared to 44.1 percent in the chemotherapy only arm. High rates of pCR were also observed in patients with stage III disease.

“Our results suggest that adding pembrolizumab to neoadjuvant chemotherapy is beneficial for patients with the most aggressive disease and the highest unmet need,” said Schmid. “I think the results have the potential to be practice-changing.”

A limitation of the study is that event-free analyses are still preliminary, as the study is ongoing. “After 15 months of follow-up, we see a strong favorable trend for event-free survival, but it has not yet met the predefined boundaries of statistical significance,” said Schmid. “Additional analyses will follow in the near future.”

This study was sponsored by MSD. Schmid has received research support from AstraZeneca, Genentech, Roche, OncoGenex Pharmaceuticals, Novartis, Astellas, and Medivation and has received honoraria or consultation funds from Pfizer, AstraZeneca, Novartis, Roche, Merck, Boehringer Ingelheim, Bayer, Eisai, Celgene, and Puma.

ABSTRACT

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Keynote-522 study of pembrolizumab + chemotherapy vs placebo + chemotherapy as neoadjuvant treatment, followed by pembrolizumab vs placebo as adjuvant treatment for early triple-negative breast cancer: Pathologic complete response in key subgroups

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Background: Previous studies have shown that the anti-PD-1 antibody, pembrolizumab (pembro) demonstrated clinical antitumor activity and had manageable side effects in patients (pts) with metastatic triple-negative breast cancer (TNBC). Immune checkpoint inhibition may enhance endogenous anticancer immunity following increased tumor-specific antigen release with chemotherapy (chemo). Results from the phase 1b KEYNOTE-173 and the phase 2 I-SPY 2 studies showed that the combination of pembro with chemo as neoadjuvant treatment had manageable side effects and promising antitumor activity in pts with locally advanced TNBC. The phase 3 KEYNOTE-522 study (NCT03036488) of pembro+chemo vs placebo+chemo as neoadjuvant therapy, followed by pembro vs placebo as adjuvant treatment in pts with early TNBC showed that neoadjuvant pembro+chemo significantly improved the pathologic complete response (pCR) rate.

Methods: From March 2017 to September 2018, 1174 pts from 21 countries were enrolled. Key eligibility criteria included age ≥ 18 years; previously untreated, early, non-metastatic, centrally confirmed TNBC (stage T1c N1-2 or T2-4 N0-2 per AJCC by investigator); and ECOG PS 0-1. Pts with bilateral or multifocal primary tumors and inflammatory breast cancers were allowed. Pts were randomized 2:1 to the experimental and control arms to receive 4 cycles of [pembro (200 mg Q3W) or placebo (normal saline)] + paclitaxel (80 mg/m² QW) + carboplatin (AUC 5 Q3W or AUC 1.5 QW) in the first 12 weeks, followed by 4 cycles of pembro/placebo + [doxorubicin (60 mg/m² Q3W) or epirubicin (90 mg/m² Q3W)]

Neoadjuvant and Adjuvant Treatment with Pembrolizumab Improves Pathologic Complete Response Rates for Patients with Triple-Negative Breast Cancer with Lymph Node Involvement

Page 3 of 3

+ cyclophosphamide (600 mg/m² Q3W) in the subsequent 12 weeks prior to surgery (neoadjuvant part). After definitive surgery, pts received radiation therapy as indicated and adjuvant pembro or placebo every 21 days for 9 cycles (adjuvant part) or until recurrence/unacceptable toxicity (whichever came first). All enrolled patients were stratified by tumor nodal status (positive vs negative), size (T1/T2 vs T3/T4), and schedule of carboplatin administration (Q3W vs QW). The dual primary endpoints are pCR rate, defined as ypT0/Tis ypN0, and EFS. Key secondary endpoints are safety, OS, and pCR rates, defined as ypT0 ypN0 and ypT0/Tis. Safety was evaluated per NCI CTCAE v4.0.

Results: pCR rates in key patient subgroups will be reported.

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