SAN ANTONIO BREAST CANCER SYMPOSIUM®

UT Health San Antonio | AACR American Association for Cancer Research | Baylor College of Medicine

December 10-14, 2019

Henry B. Gonzalez Convention Center, San Antonio, Texas, USA

HOT TOPIC:

ADDITION OF ATEZOLIZUMAB TO CHEMOTHERAPY DID NOT AFFECT PATHOLOGIC COMPLETE RESPONSE IN PATIENTS WITH EARLY HIGH-RISK AND LOCALLY ADVANCED TRIPLE NEGATIVE BREAST CANCER: EARLY RESULTS FROM THE NEOTRIP TRIAL

Addition of atezolizumab to nab-paclitaxel and carboplatin in the neoadjuvant setting did not improve pathologic complete response (pCR) in patients with early high-risk and locally advanced triple negative breast cancer (TNBC), according to early results from the NeoTRIPaPDL1 Michelangelo trial presented by Luca Gianni, MD, on Thursday morning.

"Continuous follow-up for the primary endpoint of event-free survival and other efficacy endpoints is ongoing, and molecular studies are underway," said Dr. Gianni.

Immune infiltration of TNBC has been associated with prognosis and response to chemotherapy, and PD-1/PD-L1 blockade may contribute to durable responses through immune mechanisms and when combined with chemotherapy. The Impassion130 trial had demonstrated that addition of atezolizumab to nab-paclitaxel was associated with significant improvements in progression-free and overall survival in PD-L1 positive metastatic TNBC, which prompted investigation of PD-L1 targeted therapy for TNBC in earlier stages.

Patients with early high-risk (T1cN1, T2N1, or T3N0) or locally advanced (T3N1, T4 any N, or any T and N2-3) unilateral TNBC were randomized to receive carboplatin (AUC2) and nab-paclitaxel (125 mg/m2) on days 1 and 8 and atezolizumab on day 1 of a 3-week cycle or the same regimen of carboplatin and nab-paclitaxel. Patients received 8 cycles of therapy prior to surgery. Because the primary aim of event-free survival at 5 years after randomization of the final patient was not mature at the time of the presentation, Dr. Gianni presented data on rate of pCR, a key secondary aim of the trial. Stratification variables included geographic location, disease stage (early high-risk or locally advanced), and PD-L1 expression (negative or positive immunohistochemistry as determined by central laboratory assessment with the VENTANA SP142 IHC assay).

Characteristics of the intent-to-treat population were similar between treatment groups. Approximately 49% of patients presented with locally advanced disease, and 56% of patients had PD-L1 positive disease. Most patients (87%) had clinically node-positive disease.

The rate of pCR was similar between treatment arms in the intent-to-treat population (43.5% vs 40.8% with vs without atezolizumab, p=0.66). PD-L1 expression and disease stage did not affect response to atezolizumab, although multivariate analysis showed that patients with PD-L1 positive disease were significantly more likely to achieve pCR regardless of treatment (odds ratio 2.08; 95% confidence interval 1.64-2.65), which Dr. Gianni attributed to the association between PD-L1 expression and immune cell infiltration of the tumor.

"PD-L1 expression is a direct measure of the extent of tumor infiltration by

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ISSUE 3 UPDATES

FRIDAY, DEC 13

PROGRAM UPDATES

- **7:00 - 8:45 AM**
  SPOTLIGHT SESSION 9: Detection and Treatment Response Assessment - Stars at Night
  Ballroom 1&2 - 3rd Level
- **7:00 - 8:45 AM**
  SPOTLIGHT SESSION 10: Toxicity, Tolerability & Cost - Stars at Night
  Ballroom 3&4 - 3rd Level
- **7:00 - 8:45 AM**
  POSTER SESSION 4 & Continental Breakfast
  Hall 1
- **8:45 - 9:30 AM**
  DEBATE
  Hall 3
- **9:30 - 11:30 AM**
  GENERAL SESSION
  Hall 3

POSTERS WITHDRAWN

POSTER SESSION 2

- P4-02-16
- P4-04-10
- P4-05-06
- P4-05-21
- P4-06-04
- P4-07-11
- P4-10-01
- P4-10-06
- P4-12-01
- P4-12-02
- P4-12-18
- P4-13-02
- P4-13-04
- P4-13-13
- P4-14-04
- P5-02-15
- P5-03-01
- P5-04-08
- P5-04-25
- P5-06-01
- P5-06-03
- P5-07-01
- P5-07-05
- P5-08-13
- P5-09-01
- P5-11-08
- P5-12-02
- P5-13-01
- P5-14-04

ONGOING CLINICAL TRIALS 3

- OT3-05-01
- OT3-08-01

*AT PRESS TIME

lymphocytes," said Dr. Gianni. "This may explain why the higher infiltration of the tumor, the higher the immune response to chemotherapy."

Treatment-related adverse events were similar between treatment arms except for the presence of immune-mediated adverse events (rates ranged from 0.7%-8%) and a higher rate of serious adverse events and abnormalities in liver transaminases in the atezolizumab arm.

HOT TOPIC:
TEN-YEAR FOLLOW-UP SHOWS ACCELERATED PARTIAL BREAST IRRADIATION COMPARES FAVORABLY WITH WHOLE BREAST IRRADIATION AFTER BREAST CONSERVATION SURGERY FOR PATIENTS WITH EARLY BREAST CANCER

Dr. Icro Meattini presented the results of the ten-year follow-up to the Accelerated Partial Breast Intensity-Modulated Radiation Therapy Florence Randomized Phase 3 Trial, assessing the long-term outcomes of Accelerated Partial Breast Irradiation (APBI) when compared to Whole Breast Irradiation (WBI), focusing on breast conservation surgery for patients with early breast cancer.

"Development in radiation oncology showed a fast move to Accelerated Partial Breast Irradiation," Dr. Meattini said. The study paid special attention to disease control through adequate selection of patients, and improvements in the safety profile and cosmetic outcome when attention is given to technical issues such as technique, dose, fractionation, and volume.

The Phase III trial included 520 patients forty years of age or older, in a 1:1 randomization between patients who underwent Accelerated Partial Breast Irradiation using IMRT and those who underwent Conventional Fractionation Whole Breast Irradiation (CF-WBI). The primary endpoint was Ipsilateral Breast Tumor Recurrence (IBTR); secondary endpoints included Overall Survival (OS) and Breast Cancer-Specific Survival (BCSS), occurrence of Contralateral Breast Cancer (CB), early and late toxicity, and physician-rated cosmesis.

The conclusions from the main published studies indicate that no other local control or survival data is needed to confirm that an external PBI is a valid approach to treat low-risk patients after breast cancer surgery. Further, to prevent adverse toxicity and cosmesis issues, special awareness should be paid to the technical issues involved in the delivery of PBI. In addition to those listed above, Dr. Meattini gave schedule and recovery time between fractions as examples of those technical issues.

The trial results show that a 10-year cumulative IBTR incidence in early breast cancer treated with external accelerated partial breast irradiation using intensity-modulated radiation therapy technique in 5 once-daily fractions is low and not significantly different from patients treated with conventional fractionation of whole breast irradiation. Locoregional Recurrence, Distant Metastases, Contralateral Breast Cancer, Breast Cancer Specific Survival, and Overall Survival rates were comparable to CF-WBI, and acute and late toxicity and cosmesis evaluations were significantly in favor or the APBI arm of the study.

"PBI studies results should be carefully well-interpreted among the oncology community," Dr. Meattini said. "We should be confident in using ASTRO and ESTRO PBI recommendations, and we should always consider offering PBI in case of a postmenopausal, ER-positive, node negative, pT1 breast cancer patient." All in all, he stated, "Accelerated PBI might be considered a standard alternative to WBI in low risk early breast cancer patients."

HOT TOPIC:
EXTENDED ADJUVANT THERAPY WITH LETROZOLE SIGNIFICANTLY IMPROVED DISEASE-FREE SURVIVAL IN EARLY-STAGE HORMONE RECEPTOR-POSITIVE BREAST CANCER: 10-YEAR RESULTS FROM THE NRG ONCOLOGY/NSABP B-42 TRIAL

Extended letrozole therapy was associated with a significant improvement in disease-free survival (DFS), breast cancer-free interval (BCFI), and distant recurrence (DR) in postmenopausal patients with early-stage, invasive, hormone receptor-positive breast cancer who had already received 5 years of endocrine therapy, according to 10-year data from the NRG Oncology/NSABP B-42 trial presented by Eleftherios P. Mamounas, MD, on Thursday afternoon.

Extended adjuvant endocrine therapy with an aromatase inhibitor (AI) or tamoxifen after 5 years of tamoxifen has been thought to improve DFS in early-stage breast cancer, although the optimal duration of adjuvant therapy with an aromatase inhibitor beyond 5 years is still unclear. The goal of the NSABP B-42 trial was to determine if a further 5 years of letrozole improved DFS over placebo in patients with stage I-IIIa invasive HR-positive breast cancer who were disease-free after 5 years of hormone therapy (either AI or tamoxifen followed by AI).

Patients were stratified by pathologic nodal status (negative or positive), prior adjuvant tamoxifen (yes or no), and lowest bone mineral density (BMD) T score at the spine, hip, and femur (>-2.0 or ≤-2.0 SD), and then randomized to receive letrozole or placebo for 5 years. The primary endpoint was DFS, which included local, regional, and distant recurrence; contralateral breast cancer; second non-breast primary cancer; and mortality from any cause as the first event. Key secondary endpoints included BCFI, DR, overall survival, osteoporotic fractures, and arterial thrombotic events. Analysis was based on the intent-to-treat principle, and patients were excluded if they did not have follow-up or were not at risk for the primary endpoint (metastases at the time of randomization and first non-death event ≤30 days from random assignment).

A total of 3966 patients were randomized from September 2006 to January 2010. Patient, tumor, and prior treatment characteristics did not differ between treatment groups. Approximately 34% of patients were less than 60 years of age, 57% were node-negative, and 25% had a lowest BMD score <-2.0. Prior tamoxifen use was found in 39%, and 78% had HER2-negative disease.

Seven-year results presented at SABCS 2016 and published in Lancet Oncology in 2019 showed that the beneficial effect of extended letrozole therapy on DFS did not reach statistical significance (hazard ratio [HR] 0.85, p=0.048), as a significance level of 0.0418 was used to adjust for interim analysis. However, those earlier results did show a 29% reduction in rate of BCFI events (HR 0.71, p=0.03) and 28% reduction in rate of DR events (HR=0.72, p=0.03) with extended letrozole. Letrozole did not increase risk for osteoporotic fractures, but risk for arterial thrombotic events was increased after 2.5 years of letrozole therapy.

The new 10-year results presented on Thursday showed a statistically significant reduction in DFS events with letrozole (HR 0.84, p=0.011). Of note, a 29% reduction in DR and 26% reduction in BCFI events was observed with extended letrozole therapy. Multivariate analysis showed that receipt of extended letrozole, higher BMD T score, age <60 years, negative pathologic nodes, and prior use of tamoxifen were all associated with a lower rate of DFS events. Subgroup analysis showed that letrozole yielded a significant DFS benefit in patients with positive pathologic nodes, prior use of tamoxifen, BMD T score ≤2.0, age ≥60 years, and prior mastectomy. Overall survival and rates of osteoporotic fractures and arterial thrombotic events were not different between treatment groups.

Taken together, Dr. Mamounas concluded that extended letrozole therapy may be particularly beneficial for specific groups of patients with early-stage breast cancer and that future research should focus on identifying clinical and genomic characteristics that predict response.

"Our findings continue to suggest that careful assessment of potential risks and benefits is necessary for selecting appropriate candidates in patients with early-stage breast cancer," said Dr. Mamounas. "Genomic classifiers that predict risk of late recurrence and/or benefit from extended therapy may further assist with the decision to recommend extended aromatase inhibitor therapy."

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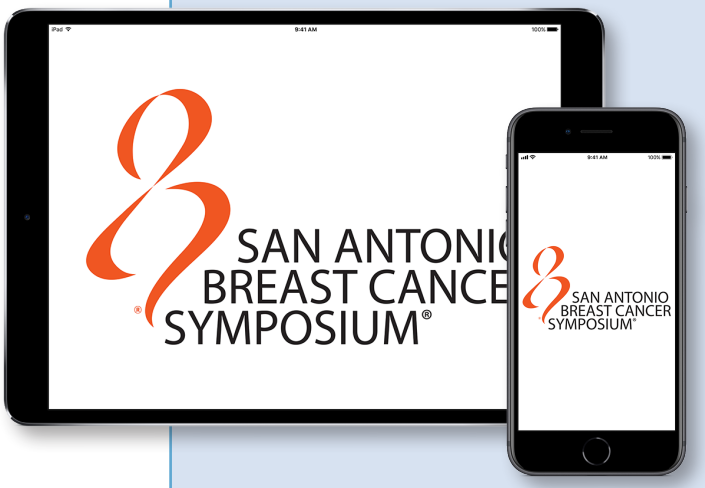

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