KEYNOTE-522: Phase 3 Study of Neoadjuvant Pembrolizumab + Chemotherapy versus Placebo + Chemotherapy, Followed by Adjuvant Pembrolizumab versus Placebo for Early Triple-Negative Breast Cancer: Pathologic Complete Response in Key Subgroups and by Treatment Exposure and Residual Cancer Burden

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KEYNOTE-522 Study Design (NCT03036488)

Stratification Factors:
- Nodal status (+ vs -)
- Tumor size (T1/T2 vs T3/T4)
- Carboplatin schedule (Q1W vs Q3W)

Key Eligibility Criteria:
- Age ≥18 years
- Newly diagnosed TNBC of either T1c N1-2 or T2-4 N0-2
- ECOG PS 0-1
- Tissue sample for PD-L1 assessment\(^a\)

Neoadjuvant phase: starts from the first neoadjuvant treatment and ends after definitive surgery (post treatment included)
Adjuvant phase: starts from the first adjuvant treatment and includes radiation therapy as indicated (post treatment included)

\(^a\)Must consist of at least 2 separate tumor cores from the primary tumor.
\(^b\)Carboplatin dose was AUC 5 Q3W or AUC 1.5 Q1W.
\(^c\)Paclitaxel dose was 80 mg/m\(^2\) Q1W.
\(^d\)Doxorubicin dose was 60 mg/m\(^2\) Q3W.
\(^e\)Epirubicin dose was 90 mg/m\(^2\) Q3W.
\(^f\)Cyclophosphamide dose was 600 mg/m\(^2\) Q1W.
Definitive pCR Analysis

- Definitive pCR analysis to test primary hypothesis of pCR based on prespecified first 602 patients (pre-calculated P value boundary for significance of 0.003)
- Consistent benefit seen with pCR defined as ypT0 ypN0 and ypT0/Tis

\[ \Delta 13.6 \ (5.4-21.8)^* \\
p = 0.00055 \]

64.8% 51.2%

\[ \text{Placebo + Chemo} \]
\[ \text{Pembro + Chemo} \]

First Pre-planned Interim Analysis for EFS

- First interim analysis of EFS based on 1174 patients: pre-calculated P value boundary for significance of 0.000051 (HR <0.4)
- Median follow-up, 15.5 months

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First Pre-planned Interim Analysis for EFS

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1 Specified P value boundary of 0.000051 not reached at this analysis (the first interim analysis of EFS). Hazard ratio (CI) analyzed based on a Cox regression model with treatment as a covariate stratified by the randomization stratification factors. Data cut-off April 24, 2019.
pCR by Disease Stage


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pCR by Lymph Node Involvement

Pre-specified analysis. Lymph node involvement was determined by the study investigator by physical exam, sonography/MRI and/or biopsy. Estimated treatment difference based on unstratified Miettinen & Nurminen method. Data cutoff date: September 24, 2018.

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![Graph showing pCR by Lymph Node Involvement]

- **Negative**: Pembro + Chemo (64.9%) vs. Placebo + Chemo (58.6%)
  - 124/91 vs. 58/99
- **Positive**: Pembro + Chemo (64.8%) vs. Placebo + Chemo (44.1%)
  - 136/210 vs. 45/102
Summary

- Neoadjuvant pembro + chemo provided a larger magnitude of pCR benefit versus chemo alone in patients with stage III and/or node positive early TNBC.
- The benefit of neoadjuvant pembro + chemo on pCR was also observed in patients who received less than the planned chemo (although absolute pCR rates were lower), and regardless of CPS threshold.
- Neoadjuvant pembro + chemo was associated with a higher rate of RCB 0-1.
- Immune-mediated adverse event rates were consistent with the known profiles of each regimen and represent no new safety concern.
- Further follow-up needed to confirm EFS benefit and the long-term safety profile.
- Additional biomarker analyses planned, including TILs and BRCA.