Practical Management Pearls for Immunotherapy for the Treatment of Breast Cancer

November 17, 2021
11:30 a.m. – 12:30 p.m. EST
Webinar Faculty

Leisha A. Emens, MD, PhD — UPMC Hillman Cancer Center

Ashley Cimino-Mathews, MD — Johns Hopkins Hospital

Sara Tolaney, MD, MPH — Dana-Farber Cancer Institute
Learning Objectives

• Describe breast cancer-specific considerations for selection and implementation of immune checkpoint inhibitors for metastatic triple-negative breast cancer

• Appropriately implement immune checkpoint inhibitors into treatment plans for early-stage triple-negative breast cancer

• Describe appropriate biomarker testing and specimen considerations for immunotherapy for triple-negative breast cancer
Webinar Outline

• Guideline development
• Advanced TNBC management
• Biomarker testing for mTNBC
• Resectable TNBC management
• Patient education and QOL
Development of the Guideline

<table>
<thead>
<tr>
<th>Society for Immunotherapy of Cancer (SITC) clinical practice guideline on immunotherapy for the treatment of breast cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leisha A Emens, Sylvia Adams, Ashley Cimino-Mathews, Mary L Disis, Margaret E Gatti-Mays, Alice Y Ho, Kevin Kalinsky, Heather L McArthur, Elizabeth A Mittendorf, Rita Nanda, David B Page, Hope S Rugo, Krista M Rubin, Hatem Soliman, Patricia A Spears, Sara M Tolaney, Jennifer K Litton</td>
</tr>
</tbody>
</table>

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Development of the Guideline

• Developed according to the Institute of Medicine’s Standards for Developing Trustworthy Clinical Practice Guidelines
• Panel consisted of 17 experts in the field
• Recommendations are based upon published literature evidence, or clinical evidence where appropriate
• Consensus was defined at 75% approval among voting members
Webinar Outline

• Guideline development
• Advanced TNBC management
• Biomarker testing for mTNBC
• Resectable TNBC management
• Patient education and QOL
Expert Panel Recommendations on anti-PD-(L)1 ICIs for Advanced TNBC

• Clinical trial enrollment remains a priority to further understand the benefit of checkpoint inhibition in metastatic breast cancer

• For patients with locally advanced/metastatic TNBC and PD-L1+ tumors by CPS score ≥10 using the 22C3 assay, pembrolizumab plus nab-paclitaxel, paclitaxel, or carboplatin and gemcitabine is recommended as one immunotherapy option for first-line treatment (LE:2), based on clinically meaningful PFS and OS improvement in KEYNOTE-355

• For patients with locally advanced/metastatic TNBC, pembrolizumab should only be added to chemotherapy (nab-paclitaxel, paclitaxel or carboplatin/gemcitabine combination) if tumors express PD-L1 with CPS≥10 by the 22C3 assay (until PD-L1 assays are harmonized) (LE: 2)

• For patients with locally advanced/metastatic TNBC and PD-L1+ tumors being treated with atezolizumab, nab-paclitaxel is the only chemotherapy backbone that has demonstrated activity in randomized clinical trials (LE: 2). The indication for atezolizumab in this setting was voluntarily withdrawn in 2021.
Rationale for Combination Immunotherapy Approaches in TNBC

Figure 1.
Immunotherapy and combination agents in triple-negative breast cancer.

Citation: Journal of the National Comprehensive Cancer Network: J Natl Compr Cancer Netw 18, 4; 10.6004/jnccn.2020.7554
Timeline of ICI Approvals and Withdrawals for TNBC

(Accelerated approval) March 2019
Atezolizumab + nab-paclitaxel for advanced PD-L1+ TNBC

(Accelerated approval) November 2020
Pembrolizumab + chemotherapy for advanced PD-L1+ TNBC

July 2021
Pembrolizumab + chemotherapy for high-risk early stage TNBC

August 2021
Atezolizumab TNBC indication voluntarily withdrawn

(Regular approval granted)
Practical Pearls on ICI Therapy for Advanced-stage Breast Cancer
### Data from Phase III Trials of ICIs for Advanced TNBC

<table>
<thead>
<tr>
<th>Trial name</th>
<th>Phase</th>
<th>Setting</th>
<th>Control and immunotherapy arms</th>
<th>Key outcome measures for FDA approval</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Trials leading to FDA approvals</strong></td>
<td></td>
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<tr>
<td>IMpassion130</td>
<td>III</td>
<td>Previously untreated TNBC</td>
<td>Control (n=451): Placebo+nab-paclitaxel</td>
<td>PD-L1 IC+</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Immunotherapy (n=451): Atezolizumab+nab-paclitaxan</td>
<td>PFS 7.5 vs 5 months</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>HR 0.62 (95% CI 0.49 to 0.78; p&lt;0.001)</td>
</tr>
<tr>
<td>KEYNOTE-355</td>
<td>III</td>
<td>Previously untreated TNBC</td>
<td>Control (n=281): Placebo+investigator’s choice: nab-paclitaxel, paclitaxel, or gemcitabine+ carboplatin</td>
<td>ITT</td>
</tr>
<tr>
<td></td>
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<td></td>
<td>Immunotherapy (n=566): Pembrolizumab+investigator’s choice: nab-paclitaxel, paclitaxel, or gemcitabine+ carboplatin</td>
<td>PFS 9.7 vs 5.6 months</td>
</tr>
<tr>
<td></td>
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<td>HR 0.65 (95% CI 0.49 to 0.86; p=0.0012)</td>
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<td>CPS≥10</td>
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<td></td>
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<td>PFS 7.6 vs 5.6 months</td>
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<td>HR 0.74 (95% CI 0.61 to 0.90; p=0.0014)</td>
</tr>
</tbody>
</table>

Data from Phase III Trials of ICIs for Advanced TNBC

<table>
<thead>
<tr>
<th>Trial</th>
<th>III</th>
<th>Status</th>
<th>Treatment Control (n=310): Investigator’s choice: capecitabine, eribulin, gemcitabine, or vinorelbine</th>
<th>CPS≥10</th>
<th>OS 10.7 vs 10.2 months</th>
<th>HR 0.86</th>
<th>(95% CI 0.69 to 1.06; p=0.0728)</th>
<th>CPS≥1</th>
<th>OS 9.9 vs 10.8 months</th>
<th>HR 0.97</th>
<th>(95% CI 0.82 to 1.15)</th>
</tr>
</thead>
<tbody>
<tr>
<td>KEYNOTE-119</td>
<td>III</td>
<td>TNBC that has progressed on prior therapy</td>
<td>Immunotherapy (n=312): Pembrolizumab</td>
<td>CPS≥10</td>
<td>OS 12.7 vs 11.6 months</td>
<td>HR 0.78</td>
<td>(95% CI 0.57 to 1.06; p=0.0574)</td>
<td>CPS≥1</td>
<td>OS 10.7 vs 10.2 months</td>
<td>HR 0.86</td>
<td>(95% CI 0.69 to 1.06; p=0.0728)</td>
</tr>
<tr>
<td>IMpassion131</td>
<td>III</td>
<td>Previously untreated TNBC</td>
<td>Control (n=220): Placebo+paclitaxel</td>
<td>PD-L1 IC+</td>
<td>PFS 6 vs 5.7 months</td>
<td>HR 0.82</td>
<td>(p=0.20)</td>
<td>ITT</td>
<td>OS 19.2 vs 22.8 months</td>
<td>HR 1.11</td>
<td>(95% CI 0.82 to 1.15)</td>
</tr>
</tbody>
</table>

ICI therapy in TMB-high solid tumors
Trials Leading to Tissue-agnostic Approvals of ICIs

<table>
<thead>
<tr>
<th>Trials leading to tissue-agnostic approvals</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pooled analysis:</strong></td>
</tr>
<tr>
<td>KEYNOTE-016</td>
</tr>
<tr>
<td>KEYNOTE-164</td>
</tr>
</tbody>
</table>

## Association between TMB and Benefit with ICIs in TNBC


<table>
<thead>
<tr>
<th>Trial</th>
<th>Agent(s) investigated</th>
<th>Number of patients evaluated for TMB (n TMB-H)</th>
<th>Outcomes: ORR; PFS HR (immunotherapy vs chemo); OS (immunotherapy vs chemo)</th>
</tr>
</thead>
<tbody>
<tr>
<td>KEYNOTE-119</td>
<td>Pembrolizumab vs chemotherapy (investigator's choice: capecitabine, eribulin, gemcitabine, or vinorelbine)</td>
<td>132 in pembrolizumab arm (n=12 TMB-H); 121 (n=14 TMB-H) in chemotherapy arm</td>
<td>TMB&gt;10mut/Mb ORR 14.3% (95% CI 4% to 39.9%) vs 12.7% (95% CI 7.9% to 19.9%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>TMB&lt;10mut/Mb ORR 8.3% (95% CI 0.4% to 35.4%) vs 12.8% (95% CI 7.8% to 20.4%)</td>
</tr>
<tr>
<td></td>
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<td></td>
<td>PFS HR 1.14 (95% CI 0.42 to 3.07)</td>
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<td></td>
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<td></td>
<td>OS HR 0.58 (95% CI 0.21 to 1.57)</td>
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<tr>
<td></td>
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<td></td>
<td>PFS HR 1.24 (95% CI 0.92 to 1.67)</td>
</tr>
<tr>
<td></td>
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<td></td>
<td>OS HR 0.81 (95% CI 0.61 to 1.07)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Trial</th>
<th>Agent(s) investigated</th>
<th>Biomarker evaluable population (median TMB 4.38 mut/Mb)</th>
<th>OS HR by TMB quartile, PD-L1 positive population (HR (95% CI))</th>
</tr>
</thead>
<tbody>
<tr>
<td>IMPassion130</td>
<td>Atezolizumab+chemotherapy vs placebo+chemotherapy</td>
<td>579 patients</td>
<td>Quartile 1 (TMB 2.63 mut/Mb) 0.69 (0.49 to 0.98)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Quartile 2 (TMB 4.39 mut/Mb) 0.59 (0.37 to 0.92)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Quartile 3 (TMB 7.02 mut/Mb) 0.37 (0.15 to 0.90)</td>
</tr>
</tbody>
</table>
Webinar Outline

• Guideline development
• Advanced TNBC management
• Biomarker testing in advanced/metastatic TNBC
• Resectable TNBC management
• Patient education and QOL
Biomarker Testing for Immunotherapy in Advanced/Metastatic TNBC

• PD-L1
• Tumor mutation burden (TMB)
• Microsatellite instability (MSI)/mismatch repair deficiency (dMMR)
PD-L1 in Advanced/Metastatic TNBC

• KEYNOTE-355: the addition of pembrolizumab to chemotherapy improved PFS and OS in patients with PD-L1\(^+\) TNBC

• PD-L1 positivity by immunohistochemistry (IHC) is defined as a combined positive score (CPS) $\geq 10$, using an FDA-approved assay

  • CPS = \(\text{number of PD-L1}^+\text{ tumor cells + number of PD-L1}^+\text{ immune cells}^a \times 100\text{ total number of tumor cells}\)

• Assay: PD-L1 IHC 22C3 pharmDx assay ("22C3 assay")

^a lymphocytes and plasma cells, located in tumor-associated stroma
Locally advanced TNBC

Metastatic TNBC to chest wall

PD-L1 IHC with the 22C3 assay

22C3 Positive (CPS >10)

22C3 Negative (CPS <10)
A Word on Atezolizumab and the SP142 assay in advanced/metastatic TNBC

• IMpassion130: the addition of atezolizumab to nab-paclitaxel improved outcomes in patients with PD-L1⁺ TNBC
• Indication was voluntarily withdrawn in 2021
• PD-L1 positivity by (IHC) is defined as an immune cell (IC) score ≥ 1
• IC score = percent of tumor area occupied by PD-L1⁺ immune cells
• Assay: Ventana PD-L1 (SP142) assay (“SP142 assay”)

a lymphocytes, plasma cells, macrophages, and neutrophils, in tumor-associated stroma
# PD-L1 IHC Assays

<table>
<thead>
<tr>
<th>Antibody clone</th>
<th>Assay</th>
<th>Platform</th>
<th>PD-L1 scoring for breast cancer</th>
<th>Companion diagnostic status</th>
<th>Companion diagnostic approval for TNBC</th>
</tr>
</thead>
<tbody>
<tr>
<td>SP142</td>
<td>VENTANA PD-L1 (SP142)</td>
<td>VENTANA</td>
<td>IC score = the percentage of the tumor area containing ICs labeling with PD-L1 at any intensity above background</td>
<td>Yes</td>
<td>IC score ≥1% indicates eligibility for atezolizumab (+ nab-paclitaxel)</td>
</tr>
<tr>
<td>22C3</td>
<td>PD-L1 IHC 22C3 pharmDx</td>
<td>Dako</td>
<td>CPS = number of PD-L1 staining cells (including TCs, lymphocytes, and macrophages), divided by the total number of viable TCs, multiplied by 100</td>
<td>Yes</td>
<td>CPS ≥10 indicates eligibility for pembrolizumab (+ chemotherapy)</td>
</tr>
<tr>
<td>28–8</td>
<td>PD-L1 IHC 28–8 pharmDx</td>
<td>Dako</td>
<td>Not applicable</td>
<td>No</td>
<td>None</td>
</tr>
<tr>
<td>SP263</td>
<td>VENTANA PD-L1 (SP263)</td>
<td>VENTANA</td>
<td>Not applicable</td>
<td>Not for breast cancer</td>
<td>None</td>
</tr>
</tbody>
</table>

CPS, combined positive score; IC, immune cell; IHC, immunohistochemistry; PD-L1, programmed death-ligand 1; TC, tumor cell; TNBC, triple-negative breast cancer.

Specimen Considerations for PD-L1 Biomarker Testing

Expert Panel recommendations:

• Although PD-L1 testing of primary lesions may not correlate with expression in metastatic disease, benefit was observed in IMpassion130 with any PD-L1+ result regardless of whether primary or metastatic tumor. **PD-L1 testing should be performed on the metastatic tumor, if available, but testing on primary tumor is acceptable (LE: 2).**

• When considering metastatic sites to test for PD-L1, it is preferable to prioritize extrahepatic\(^a\) sites or the primary tumor, if available

• PD-L1 testing should not be performed on fine needle aspirated cell-block specimens or decalcified bone

\(^a\) metastases to the liver are often non-inflamed
Measures of Genomic Instability in Advanced/Metastatic TNBC

- Tumor mutation burden (TMB)-high\(^a\) status
- Microsatellite instability (MSI)-high status
- Mismatch repair protein deficiency (dMMR)

\(^a\) TMB-high ≥ 10 mutations per megabase

Result of genomic instability:
- ~5% breast cancers

Causes of genomic instability:
- ~2% breast cancers
Cancers with high tumor mutation burden (TMB-high) have more mutations, increasing the chance that at least one will activate an immune response.

Immune cells can potentially identify cancer cells from specific markers that may be present on the cell surface due to cancer-related mutations.
Immune Checkpoint Inhibition for TMB-high, MSI-high, and dMMR Solid Tumors

• Single-agent pembrolizumab is approved for patients with TMB-high, MSI-high or dMMR advanced solid tumors, irrespective of histology

• First *tumor agnostic* approval of immunotherapy (ie, approval for advanced solid tumors of any primary site)

• TMB is included in most next-generation sequencing assays used to evaluate the presence of actionable mutations

• MSI is determined by PCR

• dMMR is determined by mismatch repair protein IHC
Expert Panel Recommendations on Biomarker Testing for Advanced TNBC

• All patients with unresectable locally advanced or metastatic TNBC should have tumor tissue tested for PD-L1 by an FDA-approved assay for breast cancer

• All patients who are candidates for immunotherapy treatment for metastatic TNBC should have tumor tissue tested for PD-L1 at least once, irrespective of line of therapy or prior immunotherapy in the adjuvant or neoadjuvant setting

• With the withdrawal of the indication for atezolizumab with nab-paclitaxel in metastatic TNBC, one companion diagnostic is approved by the FDA for PD-L1 testing in metastatic TNBC: the 22C3 assay with tumor and IC scoring by combined positive score. Benefit is seen for adding pembrolizumab to chemotherapy in patients with tumors expressing PD-L1 by CPS score ≥10 (LE: 2).

• Patients deriving clinical benefit from atezolizumab-based treatment in the absence of clinically significant toxicity or disease progression should continue on atezolizumab plus nab-paclitaxel rather than change therapy

• All patients with locally advanced or metastatic breast cancer should undergo comprehensive genomic profiling, including testing for TMB and MSI
Webinar Outline

- Introduction to the Guideline
- Advanced TNBC management
- Biomarker testing for mTNBC
- Resectable TNBC management
- Patient education and QOL
Expert Panel Recommendations on Immunotherapy for Early-stage TNBC

• For all patients with stage II and III TNBC, clinical trial enrollment should be considered if available

• For patients with high-risk early-stage TNBC, pembrolizumab in combination with chemotherapy as neoadjuvant treatment and then continued as a single agent as adjuvant treatment after surgery is a standard of care based on statistically significant and clinically meaningful improvement in EFS in KEYNOTE-522. Overall survival (OS) data is still maturing (LE: 2).

• For patients with stage II and III TNBC and no available trial, the addition of atezolizumab to standard neoadjuvant chemotherapy may be considered, although not FDA-approved at the time of publication and the IMpassion031 trial was not powered to assess EFS (LE: 2)

• Based on accumulated data to date, immunotherapy regimens for stage II and III TNBC should at least include an anthracycline and a taxane with or without carboplatin (LE: 2)
Approved and Emerging Indications for anti-PD-(L)1 ICIs in Early-stage Breast Cancer
<table>
<thead>
<tr>
<th>Trial name</th>
<th>Trial identifier</th>
<th>Phase</th>
<th>Subtype</th>
<th>Control and immunotherapy arms</th>
<th>pCR rate (95% CI) (investigational vs control)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I-SPY 2*</td>
<td>NCT01042379</td>
<td>II</td>
<td>HER2−</td>
<td>Control (n=201): paclitaxel × 4 → doxorubicin+cyclophosphamide × 4 → surgery</td>
<td>HR+/HER2−: 30% (17% to 43%) vs 13% (7% to 19%)</td>
</tr>
<tr>
<td></td>
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<td>Investigational (n=69): paclitaxel+pembrolizumab × 4 → doxorubicin plus cyclophosphamide × 4 → surgery</td>
<td>TNBC: 60% (44% to 75%) vs 22% (13% to 30%)</td>
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<td></td>
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<td>HER2−</td>
<td>Control (n=295): paclitaxel × 4 → doxorubicin+cyclophosphamide × 4 → surgery</td>
<td>HR+/HER2−: 15% (1% to 29%) vs 15% (9% to 20%)</td>
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<tr>
<td></td>
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<td></td>
<td>Investigational (n=73): paclitaxel+pembrolizumab × 4 → pembrolizumab × 4 → surgery</td>
<td>TNBC: 27% (9% to 45%) vs 27% (19% to 35%)</td>
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<td></td>
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<td></td>
<td>HER2−</td>
<td>Control (n=299): paclitaxel × 4 → doxorubicin+cyclophosphamide × 4 → surgery</td>
<td>HR+/HER2−: 28% (18% to 38%) vs 14% (9% to 19%)</td>
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<tr>
<td></td>
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<td></td>
<td>Investigational (n=74): olaparib+durvalumab+paclitaxel × 4 → doxorubicin+cyclophosphamide × 4 → surgery</td>
<td>TNBC: 47% (29% to 64%) vs 27% (20% to 34%)</td>
</tr>
</tbody>
</table>

*pCR rate in I-SPY 2 trial is estimated due to adaptive clinical trial design.
EC, epirubicin/cyclophosphamide; HER2, human epidermal growth factor receptor 2; HR, hormone receptor; ITT, intent-to-treat; LN, lymph node; NR, not reported; pCR, pathologic complete response; PD-L1, programmed death-ligand 1; TNBC, triple-negative breast cancer.
| Study       | Phase | TNBC                        | Control (n=390): paclitaxel+carboplatin+placebo → doxorubicin+cyclophosphamide/epirubicin+cyclophosphamide+placebo x 4 → surgery → placebo | ITT  
|            |       |                            |                                                                 | 63% (59.5% to 66.4%) vs 55.6% (50.6% to 60.6%) |
|            |       |                            | Investigational (n=784): paclitaxel+carboplatin+pembrolizumab → doxorubicin+cyclophosphamide/epirubicin+cyclophosphamide+pembrolizumab x 4 → surgery → pembrolizumab | PD-L1-positive  
|            |       |                            |                                                                 | 68.9% vs 54.9% |
|            |       |                            |                                                                 | PD-L1-negative  
|            |       |                            |                                                                 | 45.3% vs 30.3% |
|            |       |                            |                                                                 | LN-negative  
|            |       |                            |                                                                 | 64.9% (NR) vs 58.6% (NR) |
|            |       |                            |                                                                 | LN-positive  
|            |       |                            |                                                                 | 64.8% (NR) vs 44.1 (NR) |

<table>
<thead>
<tr>
<th>Study</th>
<th>Phase</th>
<th>Tumor Type</th>
<th>Overview</th>
<th>Treatment Group 1</th>
<th>Treatment Group 2</th>
<th>PD-L1 Status</th>
<th>ITT</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>NeoTRIPaPDL1 NCT02620280</td>
<td>III</td>
<td>TNBC</td>
<td>Control (n=142): nab-paclitaxel+carboplatin x 8 → surgery → doxorubicin+cyclophosphamide/epirubicin+cyclophosphamide x 5 FU+epirubicin+cyclophosphamide x 4</td>
<td>Investigational (n=138): nab-paclitaxel+carboplatin+atezolizumab x 8 → surgery → doxorubicin+cyclophosphamide/epirubicin+cyclophosphamide x 5 FU+epirubicin+cyclophosphamide x 4</td>
<td>ITT 43.5% (35.1% to 52.2%) vs 40.8% (32.7% to 49.4%)</td>
<td>PD-L1-negative 32.2% (NR) vs 32.3% (NR)</td>
<td>PD-L1-positive 51.9% (NR) vs 48% (NR)</td>
<td></td>
</tr>
<tr>
<td>IMpassion031 NCT03197935</td>
<td>III</td>
<td>TNBC</td>
<td>Control (n=165): placebo x 6+nab-paclitaxel x 12 → placebo+doxorubicin+cyclophosphamide x 4 → surgery → monitoring</td>
<td>Investigational (n=168): atezolizumab x 6+nab-paclitaxel x 12 → atezolizumab+doxorubicin+cyclophosphamide x 4 → surgery → atezolizumab</td>
<td>ITT 58% (50% to 65%) vs 41% (34% to 49%)</td>
<td>PD-L1-positive 69% (57% to 79%) vs 49% (38% to 61%)</td>
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</table>
Who Is a Good Candidate for Immunotherapy in the Early-stage Setting?

Expert Panel recommendations:

• For patients with stage II and III TNBC in KEYNOTE-522, patients continued immunotherapy from the neoadjuvant setting into the adjuvant setting. The potential benefits of adjuvant immunotherapy must be weighed against the potential for toxicities with treatment.

• For patients with early stage TNBC who receive pembrolizumab, serum cortisol should be tested at baseline, prior to surgery, and as clinically indicated.
Biomarker Testing for Immunotherapy for Early-stage TNBC

**Expert Panel recommendations:**

- For patients with stage II and III TNBC, improved pCR rates with either neoadjuvant pembrolizumab or atezolizumab have been observed, regardless of PD-L1 status (LE: 2)
- PD-L1 testing is not recommended for patients with early-stage breast cancer at this time (LE: 2)
- Stromal TIL assessment in primary lesions is prognostic in early TNBC and HER2+ breast cancer (LE: 1), but has not been validated to direct clinical decision-making for chemotherapy or immunotherapy
- Biomarker assessment, including repeat receptor profiles (ER/PR/HER2) and PD-L1 status as well as NGS should be considered at first relapse (LE: 3)
Webinar Outline

• Introduction to the Guideline
• Advanced TNBC management
• Biomarker testing for mTNBC
• Resectable TNBC management
• Patient education and QOL
Major Toxicities Reported in ICI Trials for Breast Cancer
<table>
<thead>
<tr>
<th>irAE</th>
<th>All grades (%)</th>
<th>Grade 3–4 (%)</th>
<th>Grade 5 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dermatologic</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pruritus, rash</td>
<td>18</td>
<td>0.5</td>
<td>0</td>
</tr>
<tr>
<td>Endocrine</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Hypothyroidism</td>
<td>12</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Hyperthyroidism</td>
<td>5</td>
<td>0.1</td>
<td>0</td>
</tr>
<tr>
<td>Gastro-intestinal</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Hepatitis, elevated transaminases</td>
<td>10</td>
<td>3</td>
<td>0.2</td>
</tr>
<tr>
<td>Colitis, diarrhea</td>
<td>2.5</td>
<td>0.45</td>
<td>0</td>
</tr>
<tr>
<td>Hematologic</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Prespecified autoimmune anemia, lymphopenia, thrombocytopenia and clotting abnormalities</td>
<td>4</td>
<td>1</td>
<td>0.2</td>
</tr>
<tr>
<td>Respiratory</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pneumonitis</td>
<td>3</td>
<td>0.5</td>
<td>0.1</td>
</tr>
<tr>
<td>Other (&lt;1%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adrenal insufficiency, type 1 diabetes, ocular, myocarditis, neurological/meningitis, nephritis/ elevated creatinine</td>
<td>&lt;1</td>
<td>&lt;0.5</td>
<td>0</td>
</tr>
</tbody>
</table>

ICI, immune checkpoint inhibitor; irAEs, immune-related adverse events; TNBC, triple-negative breast cancer.
Toxicity Considerations for Early-stage versus Advanced TNBC

**Expert Panel recommendations:**

- Patients should be monitored for symptoms of immune toxicities during immunotherapy and for at least 12 months after discontinuation of treatment. Importantly, irAEs may occur after immunotherapy has been discontinued and other therapy initiated (LE: 1)

- For patients with breast cancer who experience irAEs during immunotherapy treatment, management should generally follow the most updated guidelines (eg, SITC, ASCO, National Comprehensive Cancer Network (NCCN)) as this field is rapidly evolving

- For patients with breast cancer who develop thyroid disorders or adrenal insufficiency while on treatment, immunotherapy can generally be continued (LE: 2)
Key Considerations for Patient Education

**Expert Panel recommendations:**

• For patients receiving immunotherapy, education should be provided, including the differences between chemotherapy and immunotherapy. Whenever possible, caregivers and family members should be included in these conversations.

• Patients and providers should be educated about potential irAEs, including the expected timing of symptom onset and management of toxicity with immunotherapies, rationale for holding doses as opposed to dose reductions, and detailed parameters for when to contact their care team.

• For patients being treated with immunotherapy, education should include the importance of early recognition and management of irAEs, emphasizing that some of the more common toxicities have vague symptoms and therefore any change from baseline health should be reported. Additionally, patients should be encouraged to inform all their current and future healthcare providers that they have been treated with immunotherapy.

• Patients should be encouraged to use contraception while receiving immunotherapy, and a discussion about fertility should be initiated prior to treatment.
Conclusions

• Checkpoint inhibition + chemotherapy is a standard therapy for patients with advanced PDL1+ TNBC
  • PDL1 testing with 22C3 using CPS>=10 as a cut-off is standard for selecting patients for therapy with pembrolizumab

• Preoperative chemotherapy + checkpoint inhibition is standard of care for patients with early stage 2/3 TNBC
  • PDL1 testing is not needed to select patients for checkpoint inhibition with early stage disease

• Patients with metastatic breast cancer and high TMB (>=10 mutations/MB) are candidates for pembrolizumab monotherapy

• Further work is ongoing looking at the utility of checkpoint inhibitors with other breast cancer subtypes
Case Studies in Immunotherapy for the Treatment of Breast Cancer

December 1, 2021, 11:30 a.m. – 12:30 p.m. ET

Practical Management Pearls in Immunotherapy for the Treatment of Hepatocellular Carcinoma

December 6, 2021, 5:30 – 6:30 p.m. ET

Practical Management Pearls for Immunotherapy for the Treatment of Head and Neck Squamous Cell Carcinoma

December 9, 2021, 11 a.m. – 12 p.m. ET

Learn more and register at:
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Targets for Cancer Immunotherapy: A Deep Dive Seminar Series

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SEMINAR 7: T CELL FUNCTIONAL STATES
November 18, 2021, 4:30 – 6:30 p.m. ET

SEMINAR 8: T CELL SELECTION FOR ADOPTIVE CELL THERAPY
January 25, 2022, 11:30 a.m. – 1:30 p.m. ET

Learn more and register at: https://www.sitcancer.org/education/deepdive
Learn more and register at: https://www.sitcancer.org/aci

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A Focus on Gynecological Cancers
December 14, 2021, 12 – 4 p.m. ET
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