Case Studies in Immunotherapy for the Treatment of Breast Cancer

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

Jennifer Litton, MD – The University of Texas MD Anderson Cancer Center

Kevin Kalinsky, MD, MS – Winship Cancer Institute, Emory University

Heather McArthur, MD, MPH – UT Southwestern
Learning objectives

• Plan immunotherapy treatment regimens for challenging patient populations

• Select appropriate treatment strategies for patients with early and metastatic triple negative breast cancer

• Identify management strategies for uncommon and/or atypically responsive toxicities
Webinar outline

• Development of the guideline
• Toxicity timeframes
  • How IO differs from chemo
• Case 1: Neoadjuvant therapy- Dr. Kevin Kalinsky
• Case 2: First-line metastatic – Dr. Heather MacArthur
• Key takeaways
Development of the Guideline

<table>
<thead>
<tr>
<th>Open access</th>
<th>Position article and guidelines</th>
</tr>
</thead>
</table>

**Society for Immunotherapy of Cancer (SITC) clinical practice guideline on immunotherapy for the treatment of breast cancer**

Leisha A Emens 1, Sylvia Adams, 2 Ashley Cimino-Mathews 3, Mary L Disis, 4 Margaret E Gatti-Mays 5, Alice Y Ho, 6 Kevin Kalinsky, 7 Heather L McArthur, 8 Elizabeth A Mittendorf, 9,10 Rita Nanda, 11 David B Page 12,13 Hope S Rugo 13,14 Krista M Rubin, 14 Hatem Soliman, 15 Patricia A Spears, 16 Sara M Tolaney 17,18 Jennifer K Litton 18
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

• Development of the guideline
• Toxicity timeframes
  • How IO differs from chemo
• Case 1: Neoadjuvant therapy- Dr. Kevin Kalinsky
• Case 2: First-line metastatic – Dr. Heather MacArthur
• Key takeaways
### Toxicities Associated With Immune Checkpoint Inhibitors

<table>
<thead>
<tr>
<th>Category</th>
<th>Chemotherapy</th>
<th>Immunotherapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidence (moderate/severe AEs)</td>
<td>Almost all patients</td>
<td>Majority without</td>
</tr>
<tr>
<td>AE profile</td>
<td>Well described</td>
<td>Variable</td>
</tr>
<tr>
<td>Affected systems/organs</td>
<td>Few organs affected</td>
<td>Any organ</td>
</tr>
<tr>
<td>Time course</td>
<td>Well established</td>
<td>Variable (even after end of Tx)</td>
</tr>
<tr>
<td></td>
<td><strong>Predictable</strong></td>
<td><strong>Relatively unpredictable</strong></td>
</tr>
</tbody>
</table>

*Slide credit: clinicaloptions.com*
Organs/Systems Affected by Immune-Related Side Effects

Endocrine:
- Hyper/Hypothyroidism
- Hypophysitis
- Adrenal insufficiency
- Diabetes

Respiratory:
- Pneumonitis
- Pleuritis
- Sarcoid

Liver:
- Hepatitis

Renal:
- Nephritis

Musculoskeletal:
- Arthritis
- Dermatomyositis

Blood:
- Haemolytic Anaemia
- Thromocytopenia
- Neutropenia
- Haemophilia

Skin:
- Rash/Pruritus
- Psoriasis
- Vitiligo
- Stevens Johnston

Neurologic:
- Meningitis/Encephalitis
- Guillain Barre
- Myelopathy/neuropathy
- Myasthenia

Eye:
- Uveitis/Scleritis
- Conjunctivitis/Blepharitis
- Retinitis

Cardiovascular:
- Myocarditis
- Pericarditis
- Vasculitis

Gastrointestinal:
- Colitis
- Ileitis
- Pancreatitis
- Gastritis
Immune-Related AEs in Phase 3 TNBC Trials With CPI

* Above the incidence in the control arm
Toxicities With Immune Checkpoint Inhibitors

- Timing can be highly variable
- irAE can occur months or even a year after the end of treatment
- Time course might be even more variable with novel combinations
Multidisciplinary Management Coordinated by Oncologist
Society for Immunotherapy of Cancer (SITC) clinical practice guideline on immune checkpoint inhibitor-related adverse events

Julie R Brahmer,1 Hamzah Abu-Sbeih,2 Paolo Antonio Ascierto,3 Jill Brutsky,4 Laura C Cappelli,5 Frank B Cortazar,6,7 David E Gerber,8 Lamya Hamad,9 Eric Hansen,10 Douglas B Johnson,11 Mario E Lacouture,12 Gregory A Masters,13 Jarushka Naidoo,1,14 Michele Nanni,10 Miguel-Angel Perales,12 Igor Puzanov,10 Bianca Santomasso,15 Satish P Shanbhag,5,16 Rajeev Sharma,10 Dimitra Skondra,17 Jeffrey A Sosman,18 Michelle Turner,1 Marc S Ernstoff,19
Webinar outline

• Development of the guideline
• Toxicity timeframes
• Case 1: Neoadjuvant therapy
• Case 2: First-line metastatic
• Key takeaways
Case 1: Neoadjuvant therapy

• 44 year old woman presents with a newly diagnosed cT2N1 TNBC.
• She currently is a surgical candidate.
• What do you recommend next?
Neoadjuvant Studies: KEYNOTE-522

Eligibility
- Newly diagnosed TNBC (central confirmation)
- T1c N+ or T≥2 N0-2
- PD-L1+ or PD-L1-

Stratification
- T1/T2 vs T3/T4
- N0 vs N+
- Carboplatin Q1W vs Q3W

Study Treatment
- Neoadjuvant chemo + pembrolizumab
- Neoadjuvant chemo + placebo

Within 3-6 weeks

N = 1,174

Surgery
- Neoadjuvant chemo + pembrolizumab
- Neoadjuvant chemo + placebo

Adjuvant treatment
- Pembrolizumab 9 cycles
- Placebo 9 cycles

Primary endpoints
- pCR rate (ypT0/Tis ypN0)
- EFS

Secondary endpoints
- Alternative pCR rate (ypT0 ypN0)
- pCR rate in PD-L1+
- EFS in PD-L1+
- OS

Eligibility
- Newly diagnosed TNBC (central confirmation)
- T1c N+ or T≥2 N0-2
- PD-L1+ or PD-L1-

Surgery
- Adjuvant pembrolizumab
- Adjuvant placebo

Within 3-6 weeks

Study Treatment
- Carbo Q1W or Q3W
- Paclitaxel 80 mg/m² IV weekly
- Carboplatin weekly (AUC 1.5) or Q3W (AUC5)
- Doxorubicin 60 mg/m² IV Q3W
- Epirubicin 90 mg/m² IV Q3W
- Cyclophosphamide 600 mg/m² IV Q3W
- Pembrolizumab 200 mg IV Q3W

Eligibility
- Newly diagnosed TNBC (central confirmation)
- T1c N+ or T≥2 N0-2
- PD-L1+ or PD-L1-

Surgery
- Adjuvant pembrolizumab
- Adjuvant placebo

Within 3-6 weeks

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- Epirubicin 90 mg/m² IV Q3W
- Cyclophosphamide 600 mg/m² IV Q3W
- Pembrolizumab 200 mg IV Q3W

Eligibility
- Newly diagnosed TNBC (central confirmation)
- T1c N+ or T≥2 N0-2
- PD-L1+ or PD-L1-

Surgery
- Adjuvant pembrolizumab
- Adjuvant placebo

Within 3-6 weeks

Study Treatment
- Carbo Q1W or Q3W
- Paclitaxel 80 mg/m² IV weekly
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- Doxorubicin 60 mg/m² IV Q3W
- Epirubicin 90 mg/m² IV Q3W
- Cyclophosphamide 600 mg/m² IV Q3W
- Pembrolizumab 200 mg IV Q3W
KEYNOTE-522: pCR at IA1¹

Primary Endpoint

By PD-L1 Status

Δ 14%

Δ 14%

Δ 18%
EFS update at IA4 (39.1mo)

Events
HR (95% CI)  

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Events</th>
<th>HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pembro + Chemo/Pembro</td>
<td>15.7%</td>
<td>0.63&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Pbo + Chemo/Pbo</td>
<td>23.8%</td>
<td></td>
</tr>
</tbody>
</table>

P-value: 0.00031<sup>b</sup>

## Summary of First EFS Events by Category

<table>
<thead>
<tr>
<th>Event</th>
<th>All Subjects, N = 1174</th>
<th>Pembro + Chemo/Pembro N = 784</th>
<th>Pbo + Chemo/Pbo N = 390</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any EFS event</td>
<td></td>
<td>123 (15.7%)</td>
<td>93 (23.8%)</td>
</tr>
<tr>
<td>Progression of disease that precludes definitive surgery</td>
<td>14 (1.8%)</td>
<td>15 (3.8%)</td>
<td></td>
</tr>
<tr>
<td>Local recurrence&lt;sup&gt;a&lt;/sup&gt;</td>
<td>28 (3.6%)</td>
<td>17 (4.4%)</td>
<td></td>
</tr>
<tr>
<td><strong>Distant recurrence</strong></td>
<td><strong>60 (7.7%)</strong></td>
<td><strong>51 (13.1%)</strong></td>
<td></td>
</tr>
<tr>
<td>Secondary primary malignancy&lt;sup&gt;b&lt;/sup&gt;</td>
<td>6 (0.8%)</td>
<td>4 (1.0%)</td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>15 (1.9%)</td>
<td>6 (1.5%)</td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup> Includes local progression, local relapse, and local recurrence.

<sup>b</sup> Includes distant progression, distant relapse, and distant recurrence.

EFS by pCR (ypT0/Tis ypN0)

Overall Survival

<table>
<thead>
<tr>
<th></th>
<th>Events</th>
<th>HR (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pembro + Chemo/Pembro</td>
<td>10.2%</td>
<td>0.72&lt;sup&gt;a&lt;/sup&gt; (0.51-1.02)</td>
<td>0.03214&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Pbo + Chemo/Pbo</td>
<td>14.1%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

FDA-Approval¹

• On July 27, 2021, the FDA approved pembrolizumab for high-risk early-stage TNBC with chemotherapy as neoadjuvant treatment and then continued as a single agent as adjuvant treatment after surgery

• Based on KEYNOTE-522, the indication for palliative pembrolizumab was converted from accelerated to full approval
**IMpassion031: Phase III atezolizumab neoadjuvant study in eTNBC**

*A randomized, multicenter, international, double-blind, placebo-controlled trial*

**N = 333**
- TNBC, with primary tumour > 2 cm
- cT2-cT4, cN0-cN3, cM0
- Known PD-L1 status (IHC)
- No prior therapy for treatment or prevention of BC
- ECOG PS 0 or 1

**Stratification Factors:**
- Stage II vs Stage III
- PD-L1 IC < 1% vs IC ≥ 1%

**Co-primary endpoints:** Pathologic complete response (pCR, ypT0/is ypN0) in ITT and PD-L1–positive (IC ≥ 1%) subpopulation

**Secondary endpoints:** EFS, DFS, and OS in ITT and in PD-L1–positive subpopulation, safety, PROs

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**Treatment Arms:**
- **Placebo + nab-paclitaxel 125 mg/m² IV qw**
- **Atezolizumab 840 mg IV q2w + nab-paclitaxel 125 mg/m² IV qw**
- **Placebo + Doxorubicin 60 mg/m² IV q2w + Cyclophosphamide 600 mg/m² IV q2w**
- **Atezolizumab 840 mg IV q2w + Doxorubicin 60 mg/m² IV q2w + Cyclophosphamide 600 mg/m² IV q2w**

**12 weeks**
- **S U R G E R Y**
- **pCR ≤ 1 year from start**

**8 weeks**
- **Atezolizumab 1200 mg IV q3w x 11 doses**
- **Monitoring**

**Survival follow-up**
- ≤ 1 year from start
Co-primary endpoint pCR by PD-L1 status

**PD-L1+**

- Atezolizumab-chemo: 68.8% (53/77)
- Placebo-chemo: 49.3% (37/75)
- Δ 19.5%

**PD-L1-**

- Atezolizumab-chemo: 47.7% (42/88)
- Placebo-chemo: 34.4% (32/93)
- Δ 13.3%

Harbeck et al. ESMO 2020
Adjuvant Studies: IMpassion030

Eligibility
- Adequately excised primary invasive TNBC (stage II/III) 50:50 node negative/positive–enriched population

Stratification
- Axillary nodal status (0 vs 1-3 vs ≥4 positive lymph nodes)
- Surgery (breast conserving vs mastectomy)
- PD-L1 IC0 vs IC1/2/3

N = 2,300

Primary endpoint: iDFS in ITT
Secondary endpoints: iDFS PD-L1 IC1/2/3, OS, RFI, distant RFI, safety, and health-related QoL

Co-PIs: Ignatiadis, McArthur, Saji
Post NAC Residual Disease: SWOG 1418

**TNBC with ≥ 1 cm residual invasive breast cancer or any + LN after neoadjuvant chemotherapy**

N=100

- **Pembrolizumab 200 mg IV q 3 weeks x 1y**

1:1

- **Observation**

**Registration:**
- Central PD-L1 testing

**Stratification:**
- Nodal stage ypNo vs ypN+
- Residual tumor ≥2 vs < 2cm
- PD-L1 pos vs neg
- Prior adjuvant chemo yes vs no

**Hypothesis:**
- Pembrolizumab reduces IDFS by 33% c/w observation alone

**Primary Endpoint:**
- Invasive DFS in PD-L1-positive and overall cohort

**Secondary Endpoints:**
- Toxicity
- OS
- DRFS
- QOL (PROMIS, PRO-CTCAE forms, inflammatory markers)
- Tissue banking

Case 1, continued

- She receives neoadjuvant pembrolizumab + paclitaxel x 12 cycles followed by ddAC
- Post treatment- reveals a pCR
- Post-operatively, she develops confusion and is unable to answer questions appropriately.

- A brain MRI is unremarkable?
- What are your next steps?
Case 1, continued

• CMP, cortisol, ACTH, FSH, LH, TSH, T4
• Morning serum cortisol = 1.8 mcg/dL (Normal 10–20 mcg/dL)
• Plasma ACTH = 21 pg/mL (Normal 20–52 pg/mL)
• Very low cortisol, low-to-normal ACTH
• DS is diagnosed with secondary adrenal insufficiency (hypophysitis) and receives hydrocortisone indefinitely
Primary adrenal insufficiency

- Evaluate morning cortisol and ACTH levels
- Comprehensive metabolic panel (Na, K, CO$_2$, glucose)

Hypophysitis

- Evaluate
  - Morning cortisol and ACTH
  - FSH, LH, TSH, free T4, testosterone in men, estrogen in premenopausal women
- MRI brain ± contrast with pituitary/sellar cuts, if symptomatic
• Majority of irAEs are mild to moderate
• Severity can be asymptomatic to life-threatening; prompt recognition is crucial
• Most reversible with steroids; some require discontinuation of therapy
• Important to educate care team, patient, and caregivers on signs and symptoms of irAEs

Managing AEs From Immune Checkpoint Inhibitors

Increasing intensity of treatment required

Managed in outpatient/community setting

Generally requires Hospital admission

Increasing grade of side effect

Symptomatic therapy

<table>
<thead>
<tr>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>Moderate</td>
<td>Severe</td>
<td>Very severe</td>
</tr>
</tbody>
</table>

Referral to specialist
Strong immune suppressive treatment

Stop treatment *

Oral steroids

-----> Intravenous steroids

Steroids (PO/IV): 1-2 mg/kg/d prednisone or equivalent, slow taper over 4-6/52

* For some AEs, treatment can be restarted after resolution (e.g. rash); CPI generally continued with endocrinopathies once managed

Slide credit: clinicaloptions.com

Adapted from Champiat. ESMO Patient Guide Series.
Webinar outline

• Development of the guideline
• Toxicity timeframes
• Case 1: Neoadjuvant therapy
• Case 2: First-line metastatic
• Key takeaways
Case 2: First-line metastatic

• 41 year old woman with a BRCA1 mutation was treated with ddAC and weekly paclitaxel 2 years ago for an early stage TNBC
• She now presents with new cough and CT chest identifies multiple new lung nodules
• Biopsy of a 1.5 cm RLL nodule is consistent with metastatic TNBC
• What should you do next?
Case 2: First-line metastatic, continued

• You check PD-L1 status
  • What should you check?
**IMpassion130**

**IMpassion130** (NCT02425891): A Global, Randomized, Double-Blind, Phase 3 Study of Atezolizumab + Nab-Paclitaxel vs Placebo + Nab-Paclitaxel in Treatment-Naïve Locally Advanced or Metastatic TNBC

- Co-primary endpoints: PFS and OS in the ITT and PD-L1 populations
- Key secondary endpoints: ORR, DOR, and safety

**Stratification**
- Previously untreated metastatic or inoperable locally advanced TNBC
- ECOG PS 0-1

**N = 902**

**Atezolizumab**
- 840 mg IV on d 1 and 15 + nab-P 100 mg/m² IV on d 1, 8, and 15 of 28-d cycle until RECIST v1.1 PD
- ITT population: n = 451
- PD-L1 IC+ patients: n = 185 (41%)

**Placebo**
- 840 mg IV on d 1 and 15 + nab-P 100 mg/m² IV on d 1, 8, and 15 of 28-d cycle until RECIST v1.1 PD
- ITT population: n = 451
- PD-L1 IC+ patients: n = 184 (41%)
Interim OS Analysis

**ITT**

- 17.6 mo (15.9, 20.0)
- 21.3 mo (17.3, 23.4)

**PD-L1+**

- 15.5 mo (13.1, 19.4)
- 25.0 mo (22.6, NE)

IMpassion 130: Overall Survival

Interim OS in PD-L1+ Group

<table>
<thead>
<tr>
<th></th>
<th>Atezo + nab-P (N = 185)</th>
<th>Plac + nab-P (N = 184)</th>
</tr>
</thead>
<tbody>
<tr>
<td>OS events, n</td>
<td>64</td>
<td>88</td>
</tr>
<tr>
<td>1-year OS</td>
<td>54% (42, 65)</td>
<td>37% (26, 47)</td>
</tr>
</tbody>
</table>

OS (%)

Schmid P, et al. *ASCO 2019*

24-Month OS Rate (95% CI)

Stratified HR, 0.71*
(95% CI: 0.54, 0.93)

Patients at risk

Schmid P, et al. *ASCO 2019*

*Not formally tested due to prespecified enrichment analysis plan.
Clinical cutoff date: January 2, 2018. Median PFS (95% CI) is indicated on the plot. Median-PF (ITT): 18.0 months.
FDA-Approval

• On 3/8/19, the FDA granted accelerated approval to **atezolizumab** in combination with protein-bound paclitaxel for patients with unresectable locally advanced or metastatic TNBC whose tumors express **PD-L1** (PD-L1 stained tumor-infiltrating immune cells [IC] of any intensity covering ≥1% of the tumor area), as determined by an FDA-approved test.
FDA-Approval

- On 08/27/21, Roche withdrew the indication for atezolizumab for mTNBC
- Continued approval was contingent upon IMpassion131 trial meeting the primary PFS end point
- A potential alternative pre-market requirement is being explored
KEYNOTE-355 Study Design (NCT02819518)

Key Eligibility Criteria
- Age ≥18 years
- Central determination of TNBC and PD-L1 expression
- Previously untreated locally recurrent inoperable or metastatic TNBC
- Completion of treatment with curative intent ≥6 months prior to first disease recurrence
- ECOG performance status 0 or 1
- Life expectancy ≥12 weeks from randomization
- Adequate organ function
- No systemic steroids
- No active CNS metastases
- No active autoimmune disease

Stratification Factors:
- Chemotherapy on study (taxane vs gemcitabine/carboplatin)
- PD-L1 tumor expression (CPS ≥1 vs CPS <1)
- Prior treatment with same class chemotherapy in the neoadjuvant or adjuvant setting (yes vs no)
## Baseline Characteristics, ITT

<table>
<thead>
<tr>
<th>Characteristic, n (%)</th>
<th>All Subjects, N = 847</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pembro + Chemo N = 566</td>
</tr>
<tr>
<td>Age, median (range), yrs</td>
<td>53 (25-85)</td>
</tr>
<tr>
<td>ECOG PS 1</td>
<td>232 (41.0)</td>
</tr>
<tr>
<td>PD-L1–positive CPS ≥1</td>
<td>425 (75.1)</td>
</tr>
<tr>
<td><strong>PD-L1–positive CPS ≥10</strong></td>
<td><strong>220 (38.9)</strong></td>
</tr>
<tr>
<td>Chemotherapy on study</td>
<td></td>
</tr>
<tr>
<td>Taxane</td>
<td>255 (45.1)</td>
</tr>
<tr>
<td>Gemcitabine/Carboplatin</td>
<td>311 (54.9)</td>
</tr>
<tr>
<td>Prior same-class chemotherapy</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>124 (21.9)</td>
</tr>
<tr>
<td>No</td>
<td>442 (78.1)</td>
</tr>
<tr>
<td>Disease-free interval</td>
<td></td>
</tr>
<tr>
<td>de novo metastasis</td>
<td>167 (29.5)</td>
</tr>
<tr>
<td>&lt;12 months</td>
<td>126 (22.3)</td>
</tr>
<tr>
<td>≥12 months</td>
<td>270 (47.7)</td>
</tr>
</tbody>
</table>

Data cutoff date: December 11, 2019.
KEYNOTE-355: PFS

![Graph showing Progression-Free Survival: ITT](image)

KEYNOTE-355: PFS

**Progression-Free Survival: PD-L1 CPS ≥1**

- **56.4%** for Pembrolizumab + Chemo (n/N: 288/425, Events: 67.8%, HR (95% CI): 0.79 (0.61-0.98), P-value (one-sided): 0.00146)
- **51.7%** for Placebo + Chemo (n/N: 163/311, Events: 76.8%

Both survival curves show a decline in the percentage of patients over time. The survival rate at 7.6 months is 56.4% for Pembrolizumab + Chemo, and 51.7% for Placebo + Chemo.

**Progression-Free Survival: PD-L1 CPS ≥10**

- **65.0%** for Pembrolizumab + Chemo (n/N: 118/230, Events: 61.8%, HR (95% CI): 0.85 (0.49-0.86), P-value (one-sided): 0.00132)
- **39.1%** for Placebo + Chemo (n/N: 78/103, Events: 76.7%)

Both survival curves show a decline in the percentage of patients over time. The survival rate at 9.7 months is 65.0% for Pembrolizumab + Chemo, and 39.1% for Placebo + Chemo.

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On 11/13/20, the FDA granted accelerated approval to pembrolizumab in combination with chemotherapy for patients with unresectable or metastatic TNBC whose tumors express PD-L1 (CPS ≥10) as determined by an FDA-approved test.
Overall Survival: PD-L1 CPS ≥10

OS Δ ≈ 7 mo
# IMpassion130 PD-L1 Analysis

<table>
<thead>
<tr>
<th>Population</th>
<th>PFS</th>
<th>OS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Median PFS, mo</strong></td>
<td><strong>HR (95% CI)</strong></td>
<td><strong>Median OS, mo</strong></td>
</tr>
<tr>
<td>A + nP</td>
<td>P + nP</td>
<td>Δ</td>
</tr>
<tr>
<td>SP142+ 22C3+ (45%; 279/614)</td>
<td>8.3</td>
<td>3.9</td>
</tr>
<tr>
<td>SP142- 22C3+ (36%; 218/614)</td>
<td>7.3</td>
<td>5.6</td>
</tr>
<tr>
<td>SP142- 22C3- (18%, 111/614)</td>
<td>5.5</td>
<td>5.6</td>
</tr>
</tbody>
</table>


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Which PD-L1 Assay Should I Use?

Atezolizumab[^a]
SP142

Pembroluzimab[^b]
- TMB > 10
- MSI-H/dMMR
- CPS* score >10


* Combined Positive Score = \[
\frac{\text{# of PD-L1+ staining cells (tumor cells, lymphocytes, macrophages)}}{\text{total number of viable tumor cells}} \times 100
\]
Case 2: First-line metastatic - continued

• She has a mild rash and call your office to get instructions
After 3 weeks patient presents with G1 rash

Metastatic TNBC with lung & LN metastases

Paclitaxel + anti-PD/PD-L1

03/2018

What would you do?
1. Observe
2. Antihistamines
3. Topical steroids
4. Oral steroids

2 days later rash deteriorated to G3

What would you do?
2. Antihistamines
4. Oral steroids

Rash completely resolves after 1 week

What to do now?
1. Restart CPI

Patient with good PR until 06/2019

49
Patient presenting with new rash several weeks after starting on CPI

What to do?
1. Observe
2. Topical steroids
3. Oral steroids

Advice was given to observe

4 weeks later

63 y/o woman
Different Patterns of Skin Toxicity
Key Takeaways

• Immunotherapy has improved pCR and long term outcomes in early stage TNBC and should be considered.

• For metastatic TNBC – using as early as possible has shown improvement in PFS and OS

• Immunotoxicity patterns are different in many cases from standard expected chemotherapy toxicities.
  • Have a low threshold for evaluation as they can escalate quickly.
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