TUESDAY, OCTOBER 6, 2020

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ONQ ONCOLOGY NURSES QUALITY Improvement Series

Optimizing Treatment with Immune Checkpoint Inhibitors: The Collaborative Care of Patients with Triple Negative Breast Cancer

FACULTY

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Medical Oncologist and Hematologist
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Philadelphia, PA

PROGRAM OVERVIEW

This case-based live virtual activity will cover the treatment and management of patients with triple negative breast cancer.

TARGET AUDIENCE

This initiative is designed to meet the educational needs of U.S.-based nurse practitioners, physician assistants, clinical nurse specialists, advanced degree nurses, oncology and hematology nurses, pharmacists, and physicians involved in the treatment of patients with triple negative breast cancer (TNBC).

LEARNING OBJECTIVES

Upon completion of the program, attendees should be able to:

- Explain the complementary mechanisms found with the combination of chemotherapy and immunotherapy agents in the treatment of TNBC
- Apply evidence-based data derived from clinical trials to optimize combination regimens for the treatment of patients with metastatic TNBC
- Describe patient-centered shared decision-making approaches intended to optimize oncology care in patients with TNBC
- Discuss the roles that oncology nurses can play in the management of patients with metastatic TNBC who are treated or eligible for treatment with immunotherapy

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Purpose: This program would be beneficial for nurses involved in the management or treatment of patients with triple negative breast cancer. **CNE Credits:** 1 ANCC Contact Hour.

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The reviewer of this activity has nothing to disclose.

CNE Content Review

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1. Read the CME/CNE information and faculty disclosures
2. Participate in the live virtual activity
3. Complete the posttest and online evaluation form

You will receive your certificate as a downloadable file.

ONCOLOGY NURSES QUALITY Improvement Series

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ONCOLOGY NURSES QUALITY Improvement Series

Optimizing Treatment with Immune Checkpoint Inhibitors: The Collaborative Care of Patients with Triple Negative Breast Cancer

I. Primer in Triple-Negative Breast Cancer

a. Molecular and immunogenic characteristics of TNBC
   1. What is triple-negative breast cancer?
   2. Tumor infiltrating lymphocytes and their role
   3. ASCO-CAP classification of TNBC
b. Pathologic and clinical characteristics of TNBC
   1. The TNBC phenotype
   2. Antitumor immunity and the tumor microenvironment
c. Standard of care treatments
   1. Unmet needs

II. Combination Therapy for Metastatic TNBC – Revealing the Additive or Synergistic Effects

a. Understanding the complementary mechanisms found with the combination of chemotherapy and immunotherapy treatment
   1. How does chemotherapy augment tumor immunity?
   2. Preclinical and clinical data of chemotherapy/IO immunogenic effects
b. Mechanisms of immune modulation by chemotherapy
c. Combined anti-tumor effects of chemotherapy with checkpoint inhibition on TNBC

III. Rational Integration of Distinct Treatment Modalities for Metastatic TNBC

a. Checkpoint inhibition and its efficacy, safety in TNBC
b. Combination of IO and chemotherapy in the systemic treatment of TNBC
c. Review of current IO and chemotherapy combination clinical trials results and their use in metastatic disease

IV. Case studies

V. Multidisciplinary Oncology Team – Optimizing Patient Care and Survivorship Through Shared Decision Making

a. Benefits for patients and providers
b. Use of SDM in oncology
c. Barriers and facilitators to SDM
d. Oncology nurses as integral members of the cancer care team

VI. Conclusions and Questions and Answers

Optimizing Treatment With Immune Checkpoint Inhibitors: The Collaborative Care of Patients With Triple-Negative Breast Cancer

Sramila Aithal, MD
Chief of Medical Oncology
Medical Director, Breast Oncology
Cancer Treatment Centers of America
Philadelphia, PA

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Disclosures

- Sramila Aithal, MD is on the Speakers Bureau for Pfizer, Puma, Novartis and Seattle Genetics. Dr. Aithal has consulted for PSI-CRO.
- During the course of this lecture, Dr. Aithal may mention the use of medications for both FDA-approved and non-approved indications.

This activity is supported by an educational grant from Merck & Co., Inc.

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Learning Objectives

- Explain the complementary mechanisms found with the combination of chemotherapy and immunotherapy agents in the treatment of TNBC
- Apply evidence-based data derived from clinical trials to optimize combination regimens for the treatment of patients with mTNBC
- Describe patient-centered shared decision-making approaches intended to optimize oncology care in patients with TNBC
- Discuss the roles that oncology nurses can play in the management of patients with mTNBC who are treated or eligible for treatment with immunotherapy

mTNBC = metastatic TNBC; TNBC = triple-negative breast cancer.

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Triple-Negative Breast Cancer: An Overview

- ≈ 10%-15% of all breast cancers
- ≈ 2 times more likely in African American women before 40 years of age as compared with Caucasian or Hispanic women
- Up to 20% of TNBCs have germline *BRCA* mutation
- Shorter PFS and median survival in TNBC compared with other subtypes
- TNBC has a high likelihood of visceral metastasis, including in the brain

5-year relative survival rates in TNBC (2010-2016)	
SEER Stage	**5-Year Relative Survival Rate**
Localized	91.2%
Regional	65.0%
Distant	11.5%

PFS = progression-free survival; SEER = Surveillance, Epidemiology, and End Results.

Foulkes WD, et al. *N Engl J Med*. 2010;363:1938-1948. Centers for Disease Control and Prevention 2019 (https://www.cancer.org/cancer/breast-cancer/understanding-a-breast-cancer-diagnosis/types-of-breast-cancer/triple-negative.html). Accessed August 27, 2020. National Institutes of Health Cancer Stat Facts (https://seer.cancer.gov/statfacts/html/breast-subtypes.html). Accessed August 28, 2020. Khosravi-Shahi P, et al. *Asia Pac J Clin Oncol*. 2018;14:32-39.

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ASCO/CAP Classification of TNBC

- Hormone receptor status
  - Receptor positive: > 1% of tumor cells are positive for ER or PR
  - Receptor negative: ER and/or PR IHC expression of 0
- HER2 amplification status
  - HER2+: IHC protein expression of 3+
  - HER2-: IHC expression of 0 or 1+
  - If IHC result is 2+ (equivocal), perform dual-probe ISH
- TNBC: ER-, PR-, and HER2-

2018 ASCO/CAP dual-probe HER2 ISH interpretation

Group	*HER2*/CEP17 Ratio	*HER2* Signals/ Cell	Interpretation	Further Workup and Interpretation
1	≥ 2	≥ 4	ISH positive	
2	≥ 2	< 4	Further workup	Correlate with IHC; if 2+, count additional ISH cells HER2 NEGATIVE unless IHC 3+
3	< 2	≥ 6	Further workup	Correlate with IHC; if 2+, count additional ISH cells HER2 POSITIVE unless IHC 0 or 1+
4	< 2	≥ 4 and < 6	Further workup	Correlate with IHC; if 2+, count additional ISH cells HER2 NEGATIVE unless IHC 3+
5	< 2	< 4	ISH negative	

ER = estrogen receptor; IHC = immunohistochemistry; ISH = in situ hybridization; PR = progesterone receptor.

Hammond MEH, et al. *J Clin Oncol.* 2010;28:2784-2795. Wolff AC, et al. *J Clin Oncol.* 2018;36:2105-2122. Wolff AC, et al. *Arch Pathol Lab Med.* 2018;142:1364-1382. Foulkes WD, et al. *N Engl J Med.* 2010;363:1938-1948.

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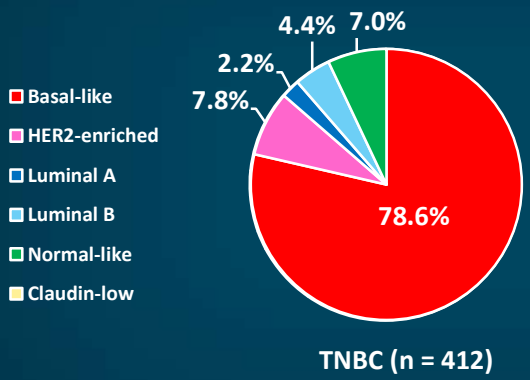
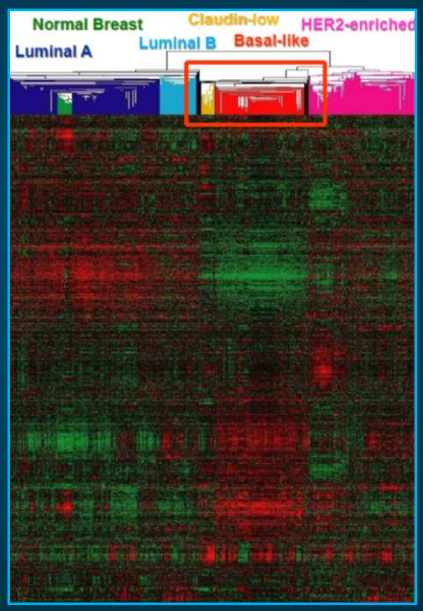
Molecular Characterization of Basal-Like and Non–Basal-Like TNBC





Prat A, et al. *Oncologist* 2013;18:123-133.

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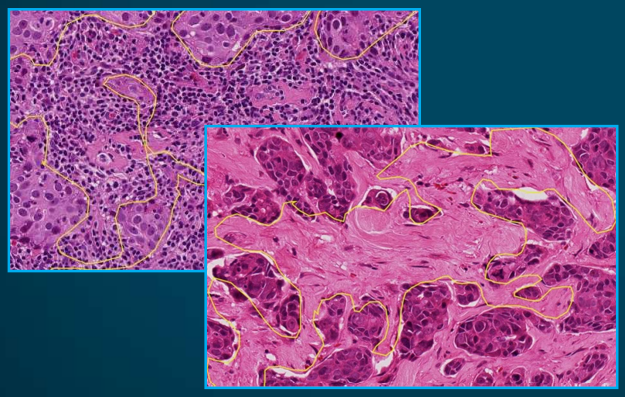
Tumor-Infiltrating Lymphocytes (TILs)

- Approximately 11% of breast cancers demonstrate LPBC
- TILs are most commonly found in highly proliferative cancers such as TNBC and HER2+ tumors
- TNBCs have the highest incidence of LPBC (range: 4%-37%)



- GeparDuo and GeparTrio trials
  - Phase 3 trials of docetaxel, doxorubicin, and cyclophosphamide combination regimens
- LPBC was defined as patients with > 60% intratumoral or stromal lymphocytes
- The *percentage of intratumoral lymphocytes* was a significant independent **predictor of pCR**, with an OR of 1.38 (95% CI: 1.08, 1.78; *P*= .012) for every 10% increase in lymphocyte infiltrate

LPBC = lymphocyte-predominant breast cancer; OR = odds ratio; pCR = pathological complete response.

Stanton SE, et al. *JAMA Oncol*. 2016;2:1354-1360. Loi S, et al. *J Clin Oncol*. 2013;31:860-867. Denkert C, et al. *J Clin Oncol*. 2010;28:105-113. Images courtesy of Carsten Denkert.

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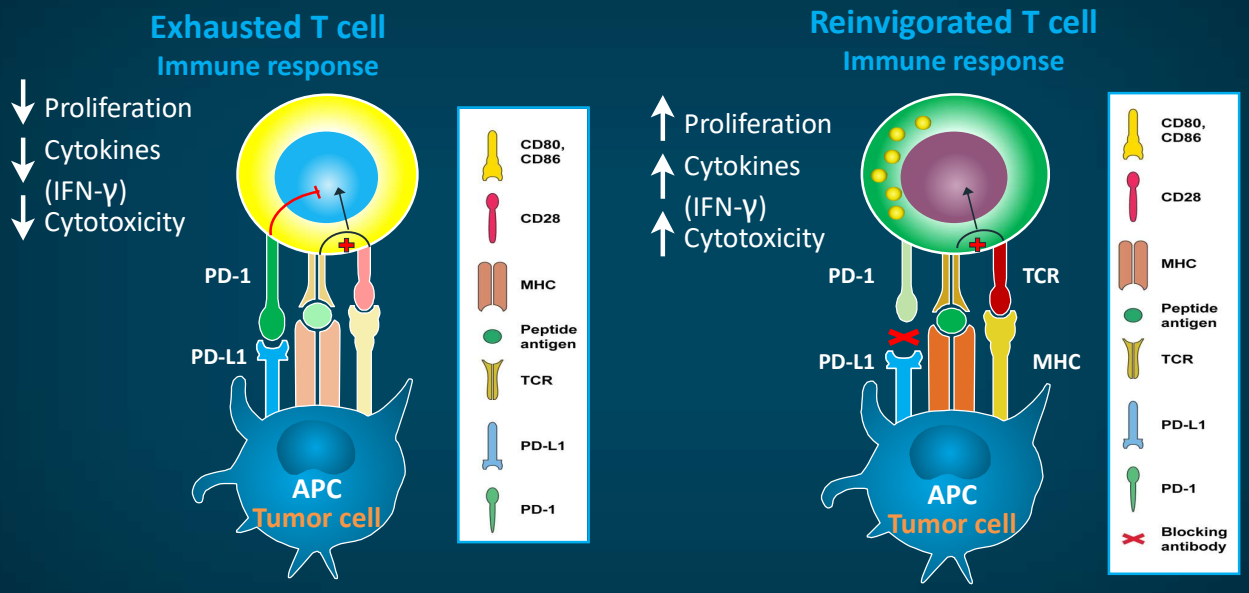
Immune Checkpoint Inhibitors: MoA



APC = antigen-presenting cells; IFN-γ = interferon-gamma; MHC = major histocompatability complex; MoA = mechanism of action; PD-1 = programmed cell death 1; PD-L1 = programmed cell death ligand 1; TCR = T-cell receptor.

Harvey RD. *Clin Pharmacol Ther*. 2014;96:214-23. Dyck L, Mills KHG. *Eur J Immunol*. 2017;47:765-779.

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Combination Therapies for Metastatic TNBC

Revealing the Additive or Synergistic Affects

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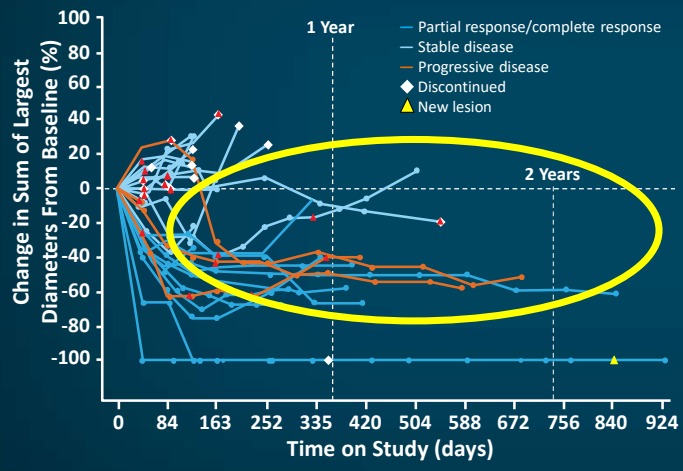
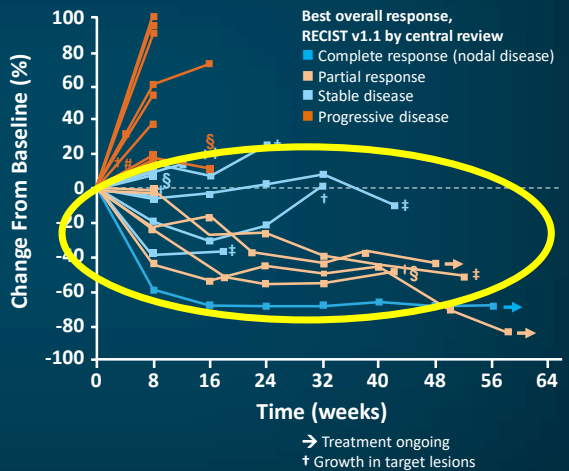
Checkpoint Blockade Confers Durable Responses… But Only a Minority of Patients Benefit

Atezolizumab (anti–PD-L1)[1,2]



Pembrolizumab (anti–PD-1)[3]



RECIST v1.1 = Response Evaluation Criteria in Solid Tumors, version 1.1.

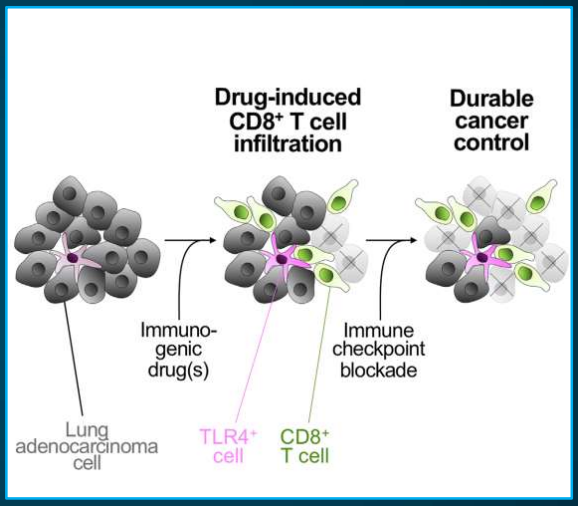
1. Schmid P, et al. AACR 2017. Abstract 2986. 2. Emens LA, et al. *JAMA Oncol.* 2019;5:74-82. 3. Nanda et al. *J Clin Oncol.* 2016;34:2460-2467.

10

Chemotherapy Can Sensitize Tumors to Checkpoint Blockade

Although chemotherapy can be immune suppressive, the ***right*** agents in the ***right*** doses at the ***right*** time can induce T-cell infiltration into tumors:

- Cyclophosphamide
- Platinums
- Anthracyclines
- Taxanes



TLR4 = toll-like receptor 4.

Pfirschke C, et al. *Immunity*. 2016;44:343-354.

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IMpassion130: Study Design

Key IMpassion 130 eligibility criteria*

- Metastatic or inoperable locally advanced TNBC
  - Histologically documented†
- No prior therapy for advanced TNBC
  - Prior chemotherapy in the curative setting, including taxanes, allowed if treatment-free interval ≥ 12 mo
- ECOG PS 0-1

Stratification factors

- Prior taxane use (yes vs no)
- Liver metastases (yes vs no)
- PD-L1 status on IC (positive [≥ 1%] vs negative [< 1%])‡

R 1:1

Atezolizumab
840 mg IV on days 1 and 15 of 28-day cycle
+ *nab*-paclitaxel
100 mg/m^2 IV on days 1, 8, and 15 of 28-day cycle

Double blind; no crossover permitted

Placebo
IV on days 1 and 15 of 28-day cycle
+ *nab*-paclitaxel
100 mg/m^2 IV on days 1, 8, and 15 of 28-day cycle

RECIST v1.1 progressive disease, or toxicity

Co-primary endpoints were PFS and OS in the ITT and PD-L1+ populations§

- Key secondary efficacy endpoints (ORR and DOR) and safety were also evaluated

*ClinicalTrials.gov: NCT02425891. †Locally evaluated per American Society of Clinical Oncology (ASCO)–College of American Pathologists guidelines. ‡Centrally evaluated per VENTANA SP142 IHC assay (double blinded for PD-L1 status). §Radiologic endpoints were investigator assessed (per RECIST v1.1). DOR = duration of response; ECOG = Eastern Cooperative Oncology Group; IC = immune cell; ITT = intention-to-treat; IV = intravenous; ORR = objective response rate; OS = overall survival; PS = performance status.

Schmid P, et al. *N Engl J Med*. 2018;379:2108-2121. Schmid P, et al. ESMO 2018. Presentation LBA1_PR.

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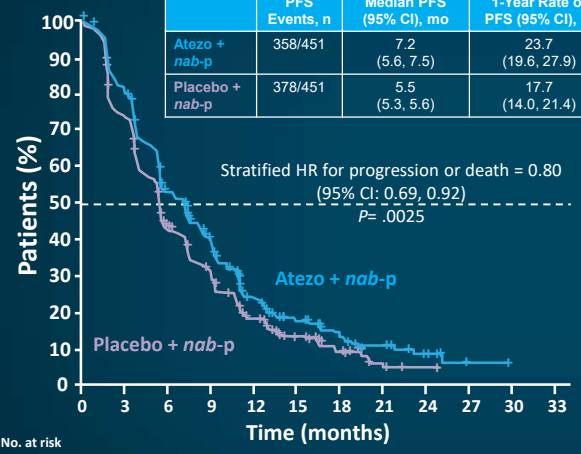
IMpassion130: Progression-Free Survival

PFS in the ITT population

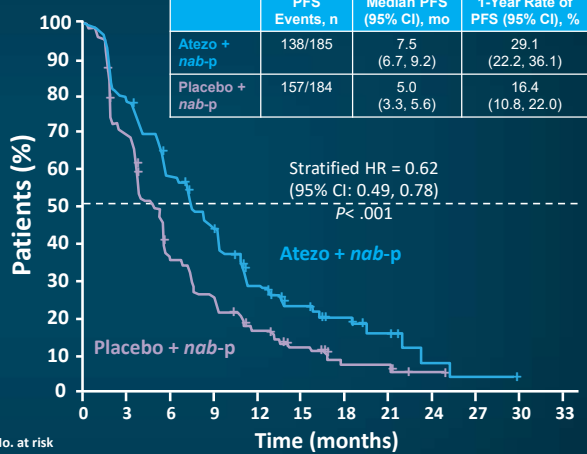
	PFS Events, n	Median PFS (95% CI), mo	1-Year Rate of PFS (95% CI), %
Atezo + *nab*-p	358/451	7.2 (5.6, 7.5)	23.7 (19.6, 27.9)
Placebo + *nab*-p	378/451	5.5 (5.3, 5.6)	17.7 (14.0, 21.4)



No. at risk												
Atezo + *nab*-p	451	360	226	164	77	34	20	11	6	1	NE	NE
Placebo + *nab*-p	451	327	183	130	57	29	13	5	1	NE	NE	NE

PFS in the PD-L1+ subgroup

	PFS Events, n	Median PFS (95% CI), mo	1-Year Rate of PFS (95% CI), %
Atezo + *nab*-p	138/185	7.5 (6.7, 9.2)	29.1 (22.2, 36.1)
Placebo + *nab*-p	157/184	5.0 (3.3, 5.6)	16.4 (10.8, 22.0)



No. at risk												
Atezo + *nab*-p	185	146	104	75	38	19	10	6	2	1	NE	NE
Placebo + *nab*-p	184	127	62	44	22	11	5	5	1	NE	NE	NE

Atezo = atezolizumab; HR = hazard ratio; *nab*-p = nab-paclitaxel; NE = not estimated.

Schmid P, et al. *N Engl J Med*. 2018;379:2108-2121.

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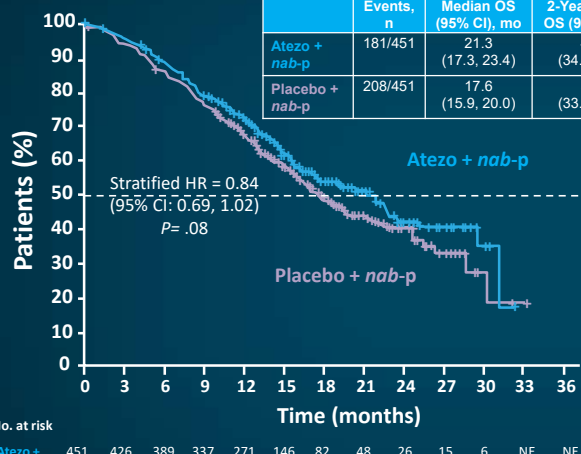
IMpassion130: Overall Survival

OS in the ITT population

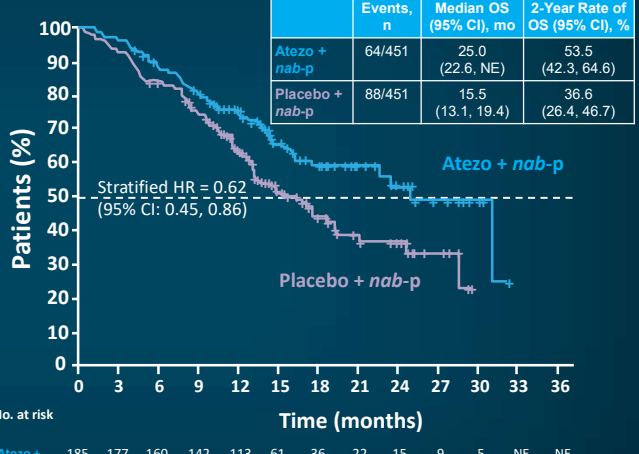
	Events, n	Median OS (95% CI), mo	2-Year Rate of OS (95% CI), %
Atezo + *nab*-p	181/451	21.3 (17.3, 23.4)	42.1 (34.3, 49.9)
Placebo + *nab*-p	208/451	17.6 (15.9, 20.0)	39.7 (33.2, 46.3)



No. at risk												
Atezo + *nab*-p	451	426	389	337	271	146	82	48	26	15	6	NE	NE
Placebo + *nab*-p	451	419	375	328	246	145	89	52	27	12	3	1	NE

OS in the PD-L1+ subgroup

	Events, n	Median OS (95% CI), mo	2-Year Rate of OS (95% CI), %
Atezo + *nab*-p	64/451	25.0 (22.6, NE)	53.5 (42.3, 64.6)
Placebo + *nab*-p	88/451	15.5 (13.1, 19.4)	36.6 (26.4, 46.7)



No. at risk												
Atezo + *nab*-p	185	177	160	142	113	61	36	22	15	9	5	NE	NE
Placebo + *nab*-p	184	170	147	129	89	44	27	19	13	6	NE	NE	NE

Schmid P, et al. *N Engl J Med*. 2018;379:2108-2121.

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IMpassion130: Adverse Events

Event	Atezolizumab + *nab*-Paclitaxel (n = 452)		Placebo + *nab*-Paclitaxel (n = 438)	
	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4
	Number of patients with event (%)			
Alopecia	255 (56.4)	3 (0.7)	252 (57.5)	1 (0.2)
Nausea	208 (46.0)	5 (1.1)	167 (38.1)	8 (1.8)
Cough	112 (24.8)	0	83 (18.9)	0
Peripheral neuropathy	98 (21.7)	25 (5.5)	97 (22.1)	12 (2.7)
Neutropenia	94 (20.8)	37 (8.2)	67 (15.3)	36 (8.2)
Pyrexia	85 (18.8)	3 (0.7)	47 (10.7)	0
Hypothyroidism	62 (13.7)	0	15 (3.4)	0

- Shown are the single most frequent AEs of any grade, AEs of any grade for which the rates differed by ≥ 5 percentage points between groups, and AEs of grade 3 or 4 for which the rates differed by ≥ 2 percentage points between groups

AE = adverse event.

Schmid P, et al. *N Engl J Med*. 2018;379:2108-2121.

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Pembrolizumab Monotherapy in Metastatic TNBC

- Pembrolizumab monotherapy showed durable antitumor activity and manageable safety in patients with mTNBC[1-4]
- Improved clinical responses observed in patients with higher PD-L1 expression[4]
- Responses to pembrolizumab monotherapy were more durable than those to chemotherapy[4]

Study	Population	N	ORR	Median DOR (range), mo	Median PFS (95% CI), mo	6-Month PFS	12-Month OS
KEYNOTE-012[1]	Heavily pretreated PD-L1–positive*	27	18.5%	NR (3.4 to 10.8+)	1.9 (1.7, 5.5)	24.4%	43.1%
KEYNOTE-086A[2]	Previously treated PD-L1–unselected	170	5.3%	NR (1.2+ to 21.5+)	2.0 (1.9, 2.0)	14.9%	39.8%
KEYNOTE-086B[3]	Previously untreated PD-L1–positive†	84	21.4%	10.4 (4.2 to 19.2+)	2.1 (2.0, 2.2)	27.0%	61.7%
KEYNOTE-119[4]	Previously treated PD-L1–selected	312	9.6%	12.2 (2.2 to 32.5+)	2.1 (2.0, 2.1)	14.7%	42.8%

*Expression in stroma or ≥ 1% of TCs by IHC and the 22C3 antihuman PD-1 antibody (Merck & Co., Kenilworth, NJ). †Assessed at a central laboratory using the PD-L1 IHC 22C3 pharmDx assay defined as the CPS, the number of PD-L1–positive cells (TCs, lymphocytes, macrophages) divided by total number of TCs x 100; PD-L1–positive = CPS ≥ 1.

CPS = combined positive score; NR = not reached.

1. Nanda R, et al. *J Clin Oncol*. 2016;34:2460-2467. 2. Adams S, et al. *Ann Oncol*. 2019;30:397-404. 3. Adams S, et al. *Ann Oncol*. 2019;30:405-411. 4. Cortes J, et al. *Ann Oncol*. 2019;30(suppl 5):v859-v860. Cortes J,et al. ASCO 2020: presentation 1000.

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Pembrolizumab Plus Chemotherapy

- Chemotherapy is a rational combination partner for anti–PD-1 therapy[1]
  - Disrupts tumor architecture and may overcome immune exclusion
  - Results in antigen shedding
  - Induces rapid disease control
- Pembrolizumab + standard neoadjuvant chemotherapy
  - Demonstrated a pCR rate of 60% across all cohorts in KEYNOTE-173[2]
  - More than doubled estimated pCR rates for HR-positive/*ERBB2*-negative and TNBC in I-SPY2[3]
  - Statistically significant increase in pCR of 13.6 percentage points (*P*= .001) vs chemotherapy alone in KEYNOTE-522[4]
  - Manageable toxicity with no unexpected safety signals[2-4]
- Pembrolizumab + chemotherapy was granted FDA breakthrough therapy designation for neoadjuvant treatment of patients with high-risk, early stage TNBC

FDA = US Food and Drug Administration; pCR = pathologic complete response.

1. Economopoulou P, et al. *Ann Oncol.* 2016;27:1675-1685. 2. Schmid P, et al. *Ann Oncol.* 2020;31:569-581. 3. Nanda R, et al. *JAMA Oncol.* 2020;6:1-9. 4. Schmid P, et al. *N Engl J Med.* 2020;382:810-821.

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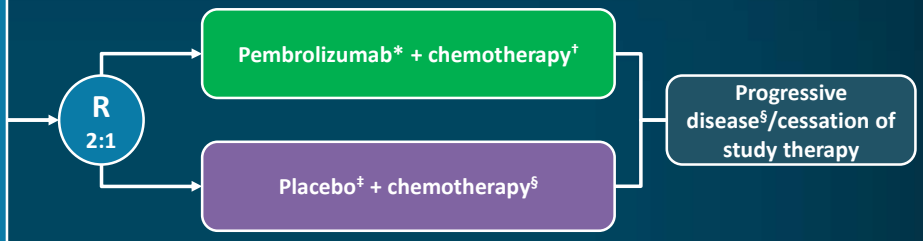
KEYNOTE-355 Study Design (NCT02819518)

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



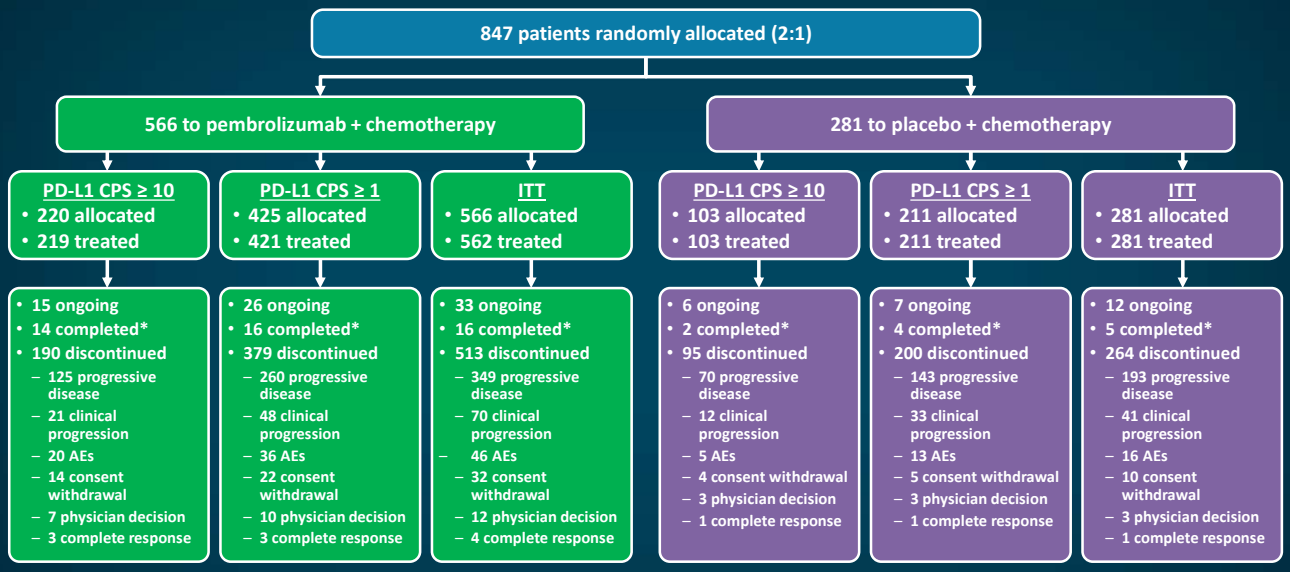
Stratification Factors:
- Chemotherapy on study (taxane vs gemcitabine/carboplatin)
- PD-L1 tumor expression (CPS ≥ 1 vs CPS < 1)
- Prior treatment with same class chemotherapy in the neoadjuvant or adjuvant setting (yes vs no)

*Pembrolizumab 200 mg IV Q3W. †Chemotherapy dosing regimens are as follows: *nab*-paclitaxel 100 mg/m² IV on days 1, 8, and 15 every 28 days; paclitaxel 90 mg/m² IV on days 1, 8, and 15 every 28 days; gemcitabine 1000 mg/m²/carboplatin AUC 2 on days 1 and 8 every 21 days. ‡Normal saline. §Treatment may be continued until confirmation of progressive disease.

AUC = area under the curve; CNS = central nervous system; Q3W = every 3 weeks.

18

Treatment Disposition of All Randomized Patients

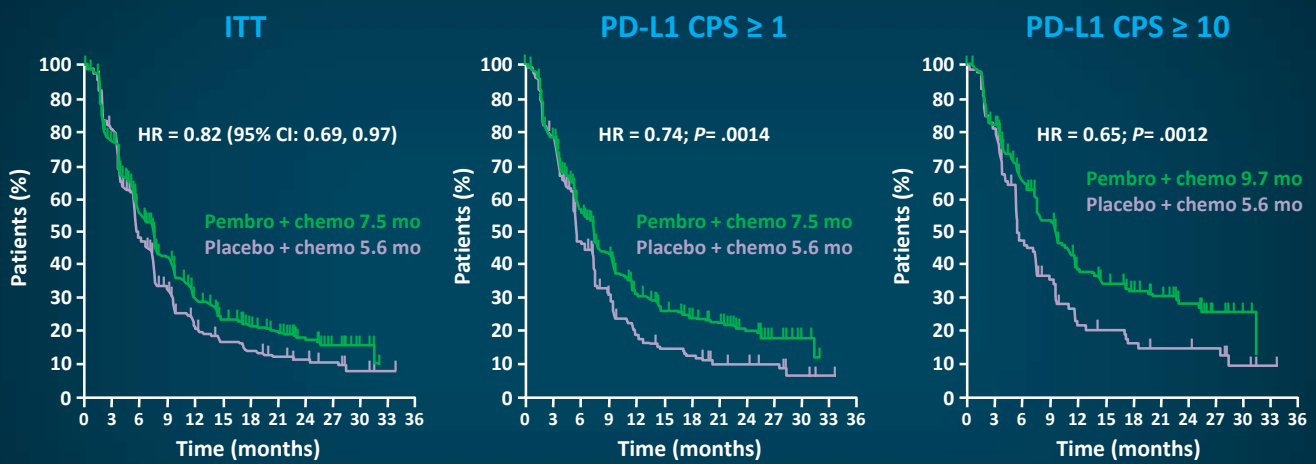


*Includes all patients who received 35 administrations of pembrolizumab or placebo and discontinued from chemotherapy; †Defined as the time from randomization to the database cutoff date of December 11, 2019.

Cortes J, et al. *J Clin Oncol.* 2020;38(15 suppl): abstract 1000. Cortes J, et al. ASCO 2020. Abstract 1000.

19

KEYNOTE 355: Progression-Free Survival



- Statistical significance was not tested due to the prespecified hierarchical testing strategy
- Prespecified *P* value boundary of .00111 not met

75% of patients

- Prespecified *P* value boundary of .00411 met

38% of patients

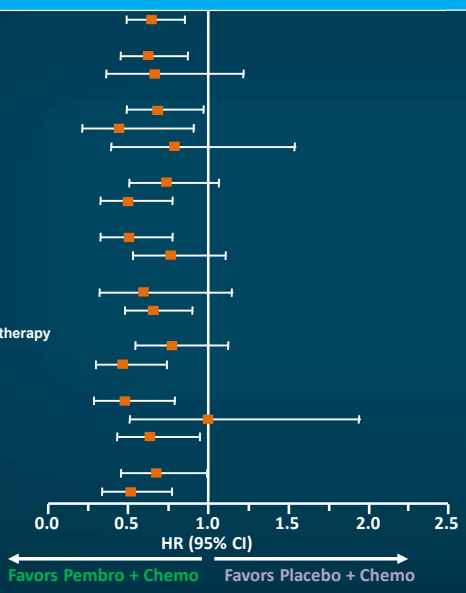
chemo = chemotherapy; Pembro = pembrolizumab.

Cortes J, et al. *J Clin Oncol.* 2020;38(15 suppl): abstract 1000. Cortes J, et al. ASCO 2020. Abstract 1000.

20

Progression-Free Survival in Subgroups: PD-L1 CPS ≥10

Subgroup	N	Median PFS, months: Pembro + Chemo	Median PFS, months: Placebo + Chemo	HR for Progression or Death (95% CI)
Overall	323	9.7	5.6	0.65 (0.49, 0.86)
Age (years)				
< 65	257	9.5	5.5	0.63 (0.46, 0.87)
≥ 65	66	10.7	7.6	0.67 (0.37, 1.23)
Geographic region				
North America/EU/ANZ	212	9.6	5.7	0.69 (0.49, 0.97)
Asia	56	17.3	5.6	0.45 (0.22, 0.91)
Rest of world	55	7.6	6.2	0.65 (0.40, 1.56)
ECOG PS				
0	196	9.8	7.5	0.74 (0.51, 1.07)
1	127	7.6	3.9	0.50 (0.33, 0.78)
On-study chemotherapy				
Taxane	143	9.9	5.4	0.51 (0.33, 0.78)
Gemcitabine/carboplatin	180	8.0	7.2	0.77 (0.53, 1.11)
Prior same-class chemotherapy				
Yes	65	7.5	5.4	0.60 (0.32, 1.15)
No	258	9.9	5.7	0.66 (0.48, 0.90)
Prior neoadjuvant/adjuvant chemotherapy				
Yes	193	7.9	5.7	0.78 (0.55, 1.12)
No	130	11.0	5.4	0.47 (0.30, 0.74)
Disease-free interval				
de novo metastasis	103	9.7	5.3	0.48 (0.29, 0.79)
< 12 months	66	7.5	7.2	1.00 (0.51, 1.95)
≥ 12 months	153	9.9	6.6	0.64 (0.43, 0.95)
Number of metastatic sites				
< 3	184	11.8	9.0	0.68 (0.46, 1.00)
≥ 3	138	7.6	4.5	0.52 (0.34, 0.78)



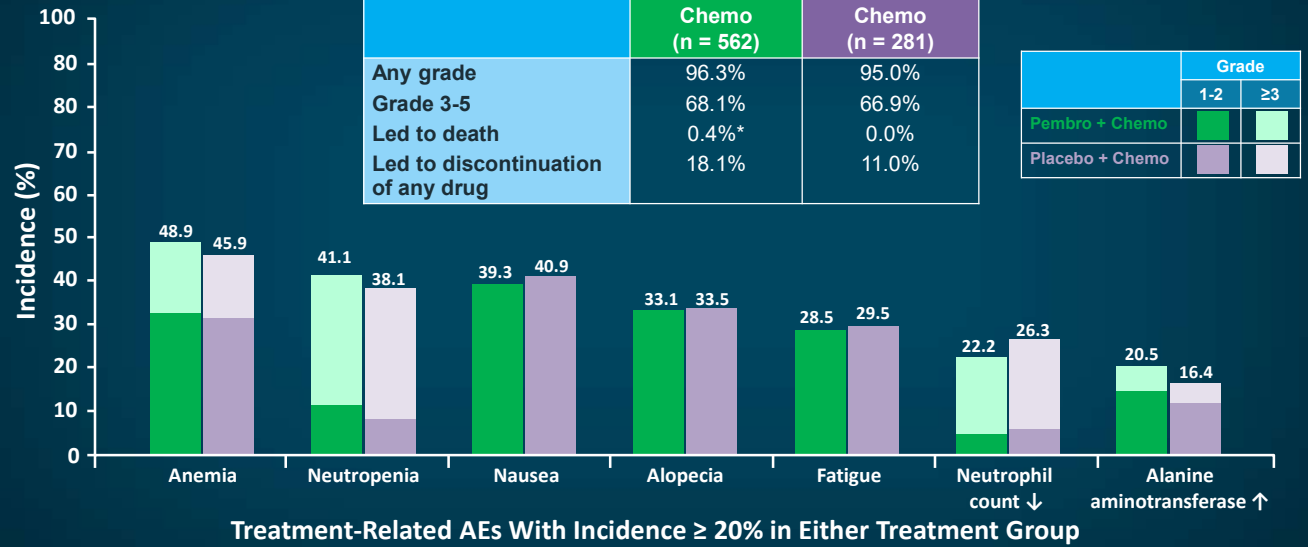
Cortes J, et al. *J Clin Oncol.* 2020;38(15 suppl): abstract 1000. Cortes J, et al. ASCO 2020. Abstract 1000.

Data cutoff date: December 11, 2019.

21

Treatment-Related AEs

All Treatment-Related	Pembro + Chemo (n = 562)	Placebo + Chemo (n = 281)
Any grade	96.3%	95.0%
Grade 3-5	68.1%	66.9%
Led to death	0.4%*	0.0%
Led to discontinuation of any drug	18.1%	11.0%



Treatment-Related AEs With Incidence ≥ 20% in Either Treatment Group

*1 patient from acute kidney injury and 1 patient from pneumonia. Data cutoff date: December 11, 2019.

Cortes J, et al. *J Clin Oncol.* 2020;38(15 suppl): abstract 1000. Cortes J, et al. ASCO 2020. Abstract 1000.

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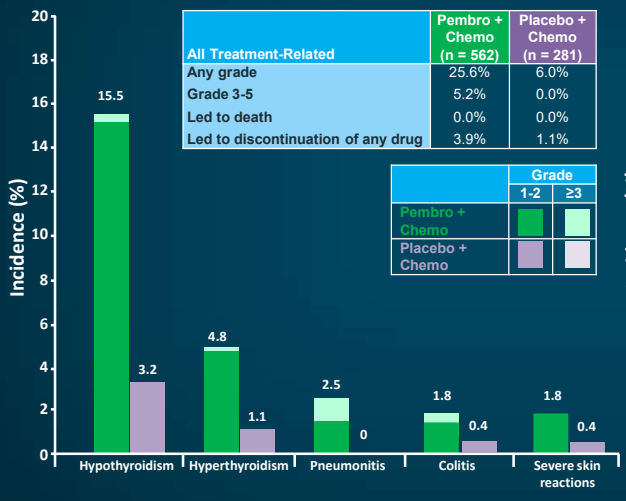
Immune-Mediated AEs With Pembrolizumab

KEYNOTE-355 immune-mediated AEs

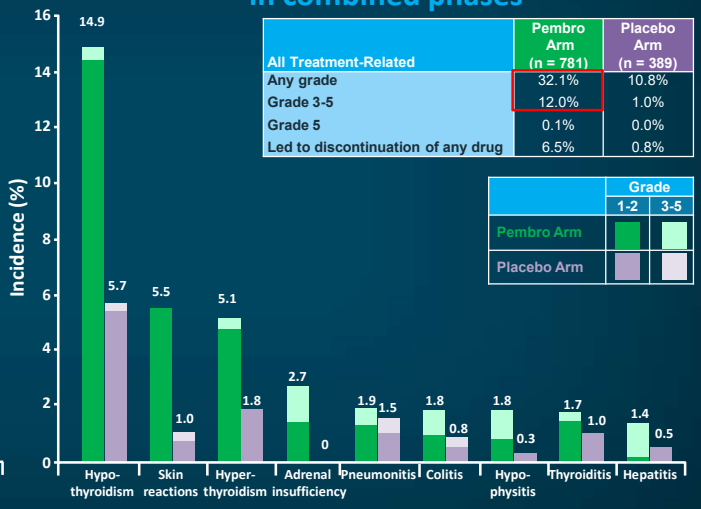
All Treatment-Related	Pembro + Chemo (n = 562)	Placebo + Chemo (n = 281)
Any grade	25.6%	6.0%
Grade 3-5	5.2%	0.0%
Led to death	0.0%	0.0%
Led to discontinuation of any drug	3.9%	1.1%



Treatment-Related AEs With Incidence ≥ 10 in Either Treatment Group

KEYNOTE-522 immune-mediated AEs in combined phases

All Treatment-Related	Pembro Arm (n = 781)	Placebo Arm (n = 389)
Any grade	32.1%	10.8%
Grade 3-5	12.0%	1.0%
Grade 5	0.1%	0.0%
Led to discontinuation of any drug	6.5%	0.8%



Immune-Mediated AEs With Incidence ≥ 10 Patients

Cortes J, et al. *J Clin Oncol.* 2020;38(15 suppl): abstract 1000. Schmid P, et al. ESMO 2019. Abstract LBA8_PR.

23

KEYNOTE-355: Summary

- Pembrolizumab + chemotherapy resulted in a statistically significant and clinically meaningful improvement in PFS vs chemotherapy alone for the first-line treatment of PD-L1–positive (CPS ≥ 10) mTNBC
- A trend toward improved efficacy with PD-L1 enrichment was observed in patients treated with pembrolizumab + chemotherapy
- Improvement in PFS was observed across patient subgroups
- Safety was consistent with the known profiles of each regimen
- These findings suggest a role for the addition of pembrolizumab to standard chemotherapy for the first-line treatment of mTNBC

Cortes J, et al. *J Clin Oncol.* 2020;38(15 suppl): abstract 1000. Cortes J, et al. ASCO 2020. Abstract 1000.

24

Where to Draw the Line for Neoadjuvant Immunotherapy?

Are the current trial data supportive of using immunotherapy in the neoadjuvant setting?

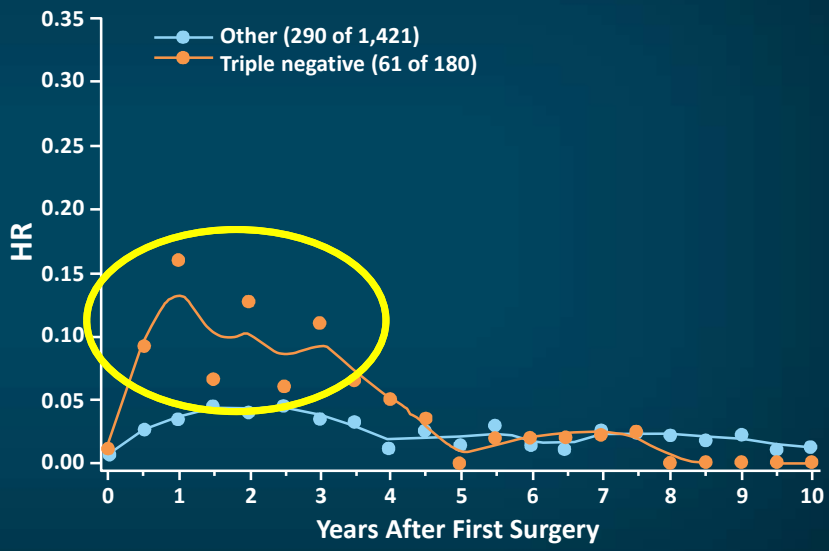
- Is improvement in pCR alone adequate?
- What about the increased rate of immune-mediated AEs?

Hamilton E. ASCO 2020.

25

Moving Immune Checkpoint Inhibitors Into the Curative-Intent Setting for TNBC

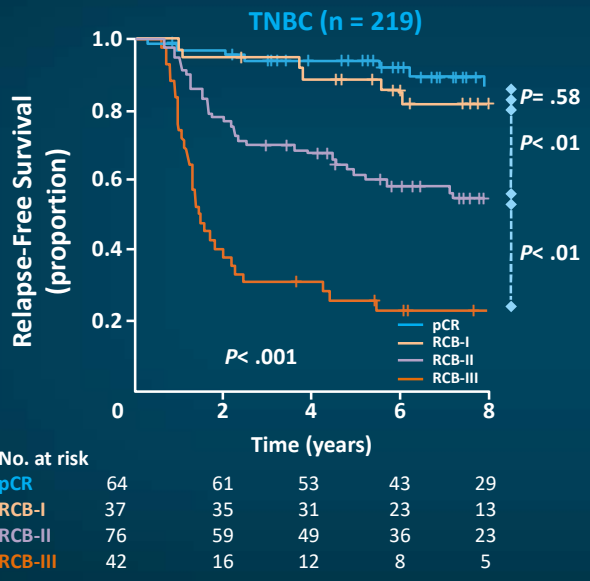
- Recurrence risk occurs early for TNBC
- Median OS for mTNBC (treated with conventional cytotoxic therapy) = 9–12 months



Dent R, et al. *Clin Cancer Res*. 2007;13:4429-4434. Khosravi-Shahi P, et al. *Asia Pac J Clin Oncol*. 2018;14:32-39.

26

Recurrence in TNBC Correlates With Volume of Residual Disease



No. at risk

pCR	64	61	53	43	29
RCB-I	37	35	31	23	13
RCB-II	76	59	49	36	23
RCB-III	42	16	12	8	5

Proportion of patients

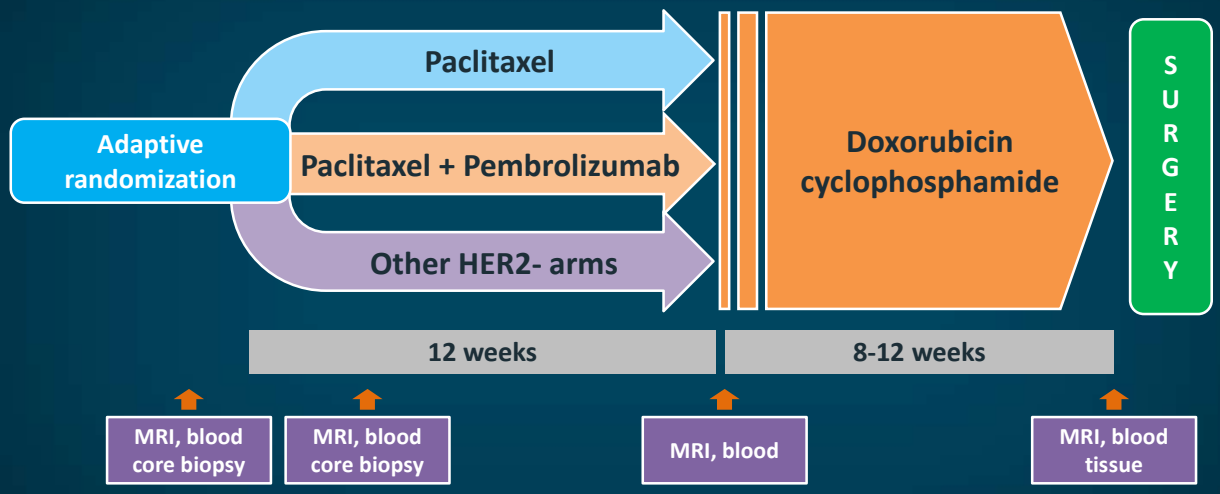
pCR	35%
RCB-I	15%
RCB-II	33%
RCB-III	17%

RCB = residual cancer burden.

Symmans WF, et al. *J Clin Oncol.* 2017;35:1049-1060.

27

I-SPY2 TRIAL Schema: HER2- Signatures



Nanda R, et al. ASCO 2017. Abstract 506.

28

Pembrolizumab Graduated in All HER2- Signatures: Both HR+/HER2- and Triple Negative

Signature	Estimated pCR Rate (95% PI)		Probability Pembrolizumab Is Superior to Control	Predictive Probability of Success in Phase 3
	Pembrolizumab	Control		
All HER2-	**0.46** (0.34-0.58)	0.16 (0.06-0.27)	> 99%	99%
TNBC	**0.60** (0.43-0.78)	**0.20** (0.06-0.33)	> 99%	> 99%
HR+/HER2-	**0.34** (0.19-0.48)	**0.13** (0.03-0.24)	> 99%	88%

- The Bayesian model estimated pCR rates appropriately adjust to characteristics of the I-SPY2 population
- The raw pCR rates (not shown) are higher than the model estimate of 0.604 in TNBC

PI = probability interval.
Nanda R, et al. ASCO 2017. Abstract 506.

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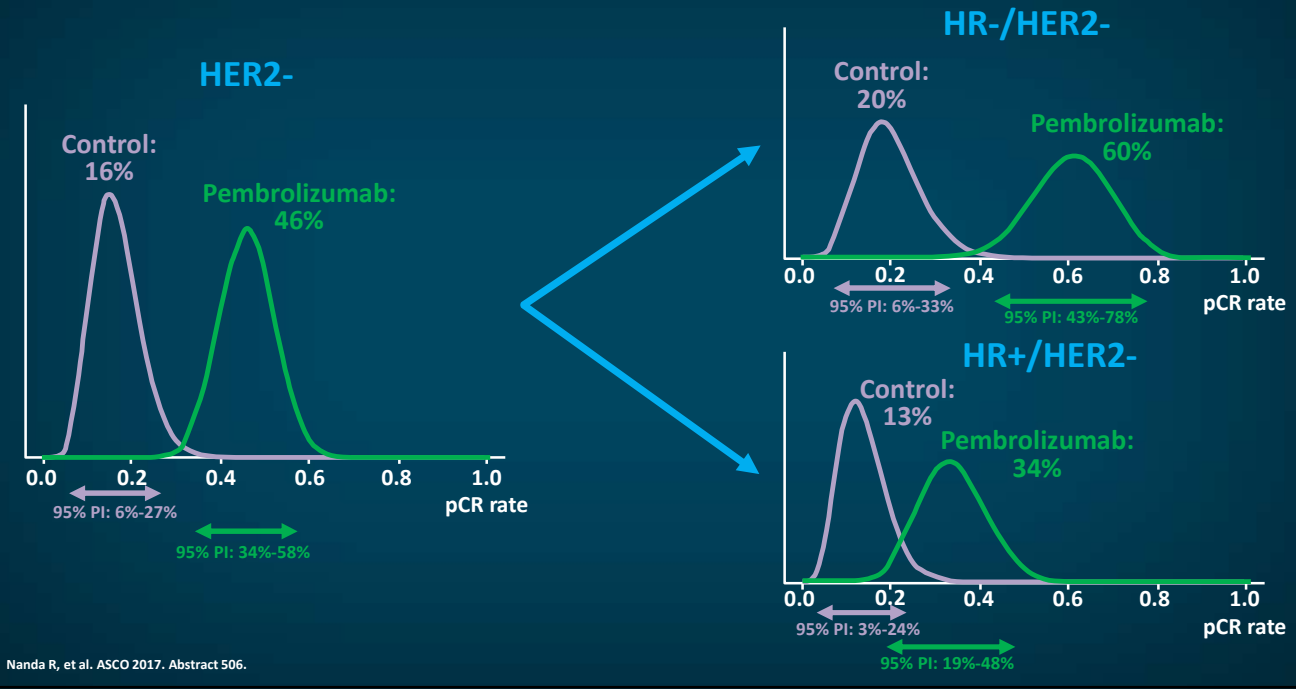
pCR Probability Distributions by Signature



Nanda R, et al. ASCO 2017. Abstract 506.

30

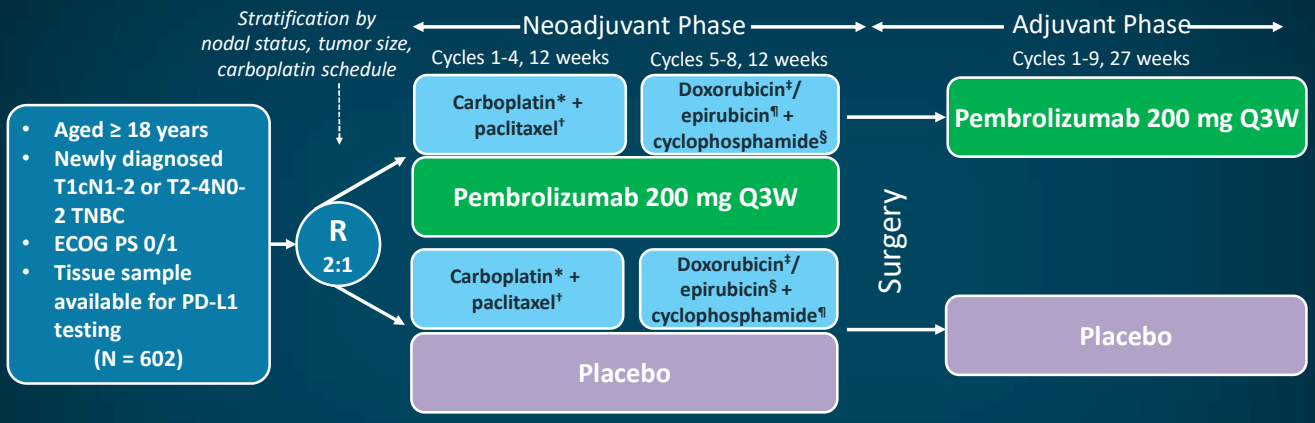
I-SPY2: Summary

- Pembrolizumab x 4 cycles + paclitaxel has graduated for all HER2- signatures studied
  - **Tripling** of the estimated pCR rate in TNBC (60% vs 20%)
  - **Near tripling** of the estimated pCR rate in HR+/HER2- (34% vs 13%)
  - First agent to graduate in HR+/HER2- signature
- Adrenal insufficiency was observed at a higher rate than previously reported in advanced cancer; patients are doing well on replacement therapy; follow-up of patient outcomes is ongoing
- This is the first report regarding the incidence and time course of immune-mediated toxicities in early stage breast cancer

Nanda R, et al. ASCO 2017. Abstract 506.

31

KEYNOTE-522: Study Design



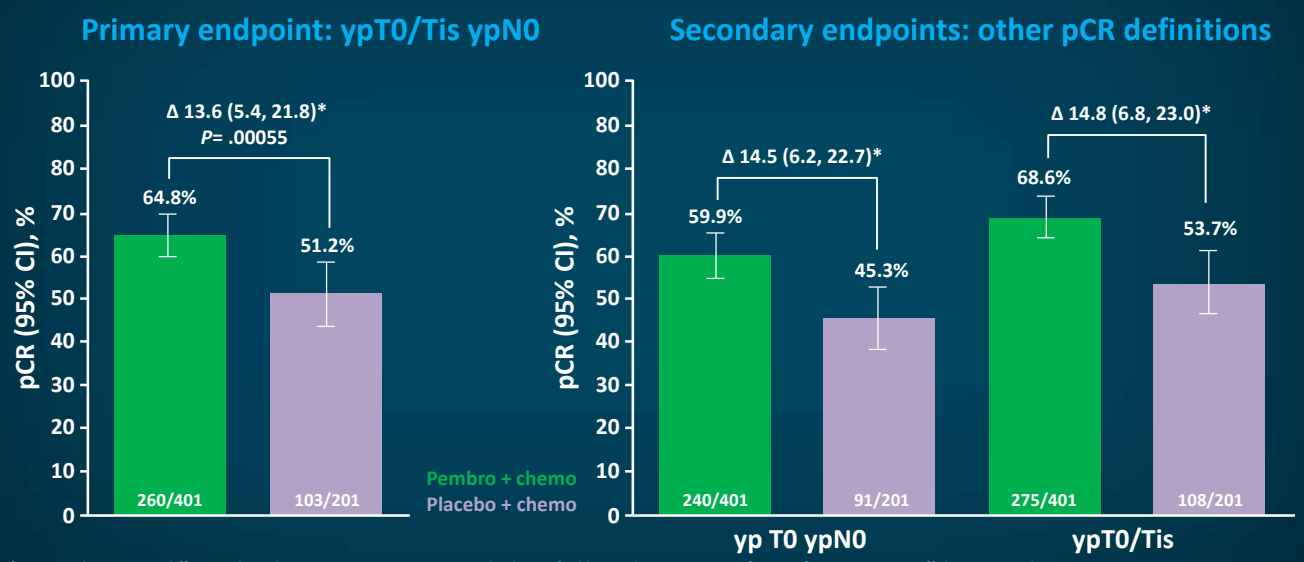
- Primary endpoints: pCR (ypT0/Tis ypN0) by local review, EFS by local review
- Secondary endpoints: pCR (ypT0 ypN0 and ypT0/Tis), OS, EFS, AE
- Exploratory endpoints: RCB, pCR by subgroups, EFS by pCR

*AUC 5 Q3W or AUC 1.5 QW. †80 mg/m² QW. ‡60 mg/m² Q3W. §90 mg/m² Q3W. ¶600 mg/m² Q3W.
EFS = event-free survival; QW = every week.

Schmid P, et al. SABCS 2019. Abstract GS3-03.

32

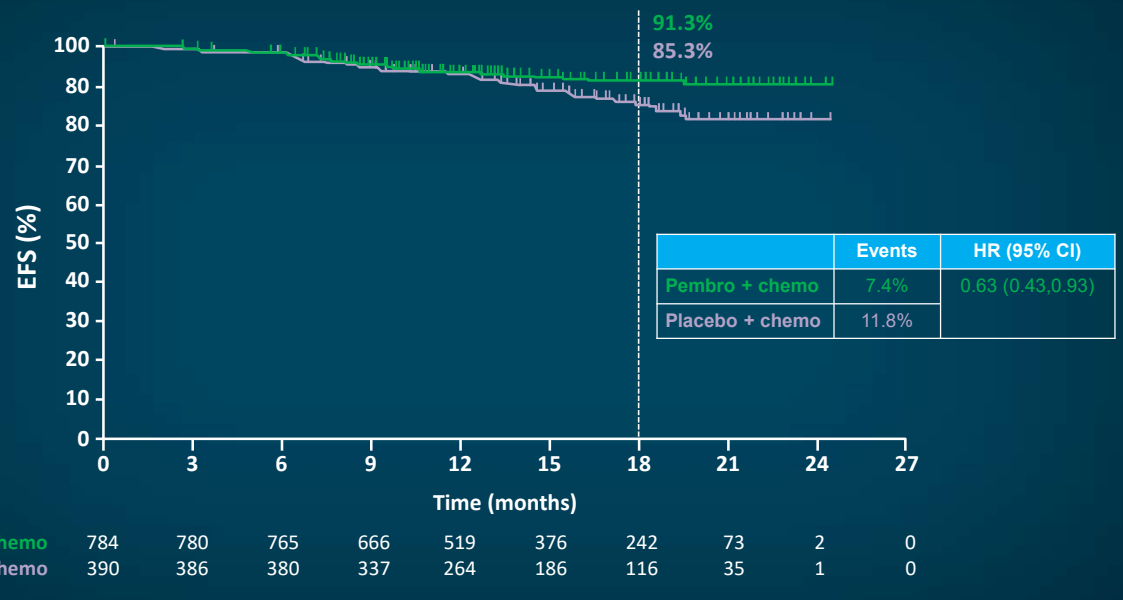
Pathological Complete Response at IA1



*Estimated treatment difference based on Mettinen & Nurminen method stratified by randomization stratification factors. Data cutoff date: September 24, 2018.
yp = postneoadjuvant pathological stage; IA1 = first interim analysis.
Schmid P, et al. SABCS 2019. Abstract GS3-03.

33

Event-Free Survival at IA2



	Events	HR (95% CI)
Pembro + chemo	7.4%	0.63 (0.43,0.93)
Placebo + chemo	11.8%	

HR (CI) analyzed based on Cox regression model with treatment as a covariate stratified by the randomization stratification factors. Data cutoff date: April 24, 2019.
Schmid P, et al. SABCS 2019. Abstract GS3-03.

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KEYNOTE-522: pCR by Key Patient Subgroups

pCR, % (n/N)		Pembrolizumab + Chemotherapy (n = 401)	Placebo + Chemotherapy (n = 201)	Δ (95% CI)
Disease stage	▪ IIA ▪ IIB ▪ IIIA ▪ IIIB	73.1 (133/182) 56.2 (68/121) 66.7 (40/60) 48.6 (18/37)	62.1 (54/87) 48.4 (30/62) 42.1 (16/38) 23.1 (3/13)	11.0 (-0.7, 23.2) 7.8 (-7.4, 22.8) 24.6 (4.3, 43.1) 25.6 (-6.1, 48.9)
Lymph node involvement	▪ Negative ▪ Positive	64.9 (124/191) 64.8 (136/210)	58.6 (58/99) 44.1 (45/102)	6.3 (-5.3, 18.2) 20.6 (8.9, 39.1)
PD-L1 expression	▪ CPS < 1 ▪ CPS ≥ 1 ▪ CPS ≥ 10 ▪ CPS ≥ 20	45.3 (29/64) 68.9 (230/334) 77.9 (162/208) 81.7 (103/126)	30.3 (10.33) 54.9 (90/164) 59.8 (55/92) 62.5 (40/64)	18.3 (-3.3, 36.8) 14.2 (5.3, 23.1) 17.5 (6.2, 29.1) 18.5 (5.0, 32.7)
Chemotherapy exposure*	▪ Full exposure ▪ < Full exposure	69.7 (314/307) 51.1 (46/90)	55.3 (88/159) 35.7 (15/42)	14.4 (5.1, 3.6) 15.4 (-3.0, 32.1)

*Full exposure comprised paclitaxel weekly 10-12 doses, carboplatin weekly 10-12 doses or Q3W 4 doses, doxorubicin or epirubicin Q3W 4 doses, and cyclophosphamide Q3W 4 doses, regardless of exposure to pembrolizumab.

Schmid P, et al. SABCS 2019. Abstract GS3-03.

35

KEYNOTE-522: Summary

- In TNBC stage II and III, neoadjuvant therapy with pembrolizumab + chemotherapy is associated with larger pCR benefit than chemotherapy alone
- Benefit is noted regardless of PD-L1 expression or completion of chemotherapy
- No new safety signals observed in the arm that received immunotherapy and side effects were consistent with prior studies
- Additional follow-up studies are necessary to confirm EFS benefit and long-term safety profile

Schmid P, et al. SABCS 2019. Abstract GS3-03.

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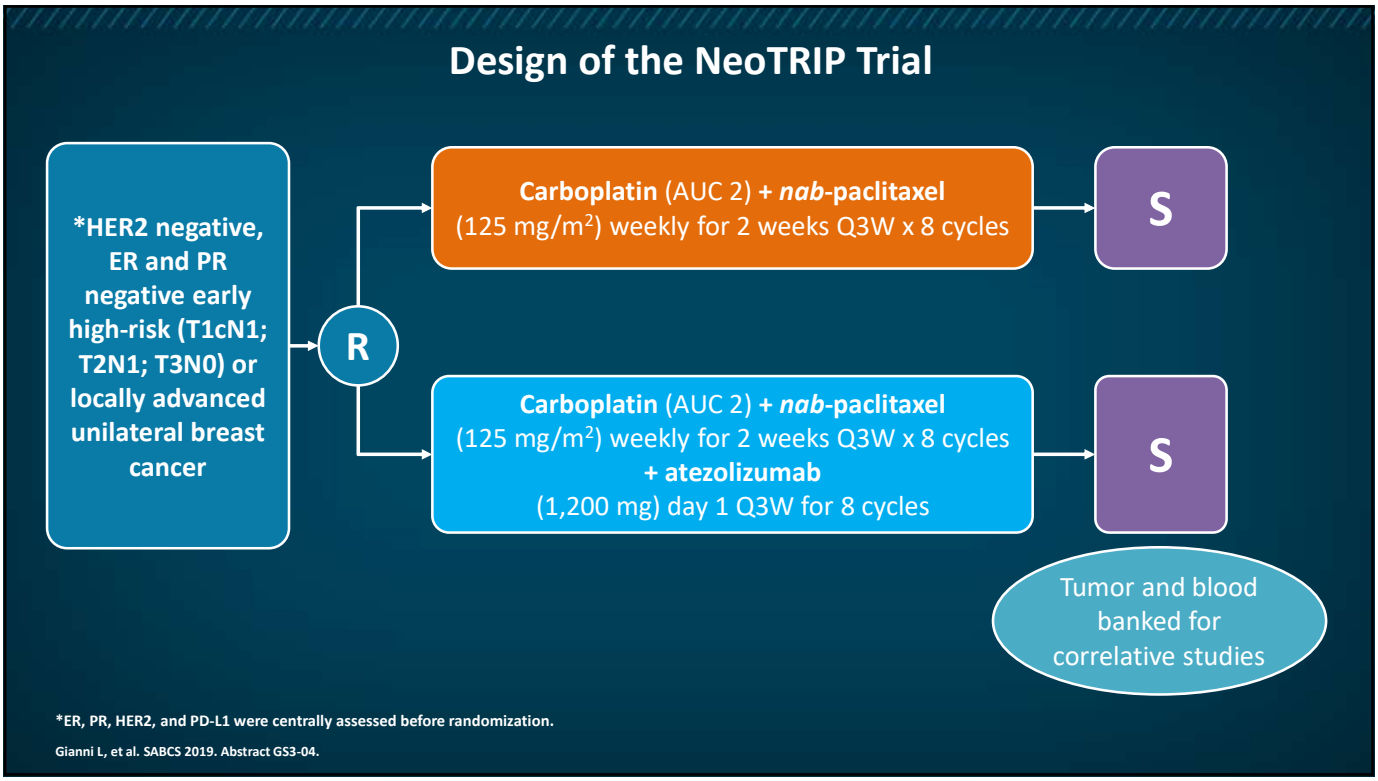
Design of the NeoTRIP Trial
*HER2 negative, ER and PR negative early high-risk (T1cN1; T2N1; T3N0) or locally advanced unilateral breast cancer
R
Carboplatin (AUC 2) + nab-paclitaxel (125 mg/m2) weekly for 2 weeks Q3W x 8 cycles
S
Carboplatin (AUC 2) + nab-paclitaxel (125 mg/m2) weekly for 2 weeks Q3W x 8 cycles + atezolizumab (1,200 mg) day 1 Q3W for 8 cycles
S
Tumor and blood banked for correlative studies
*ER, PR, HER2, and PD-L1 were centrally assessed before randomization.
Gianni L, et al. SABCS 2019. Abstract GS3-04.

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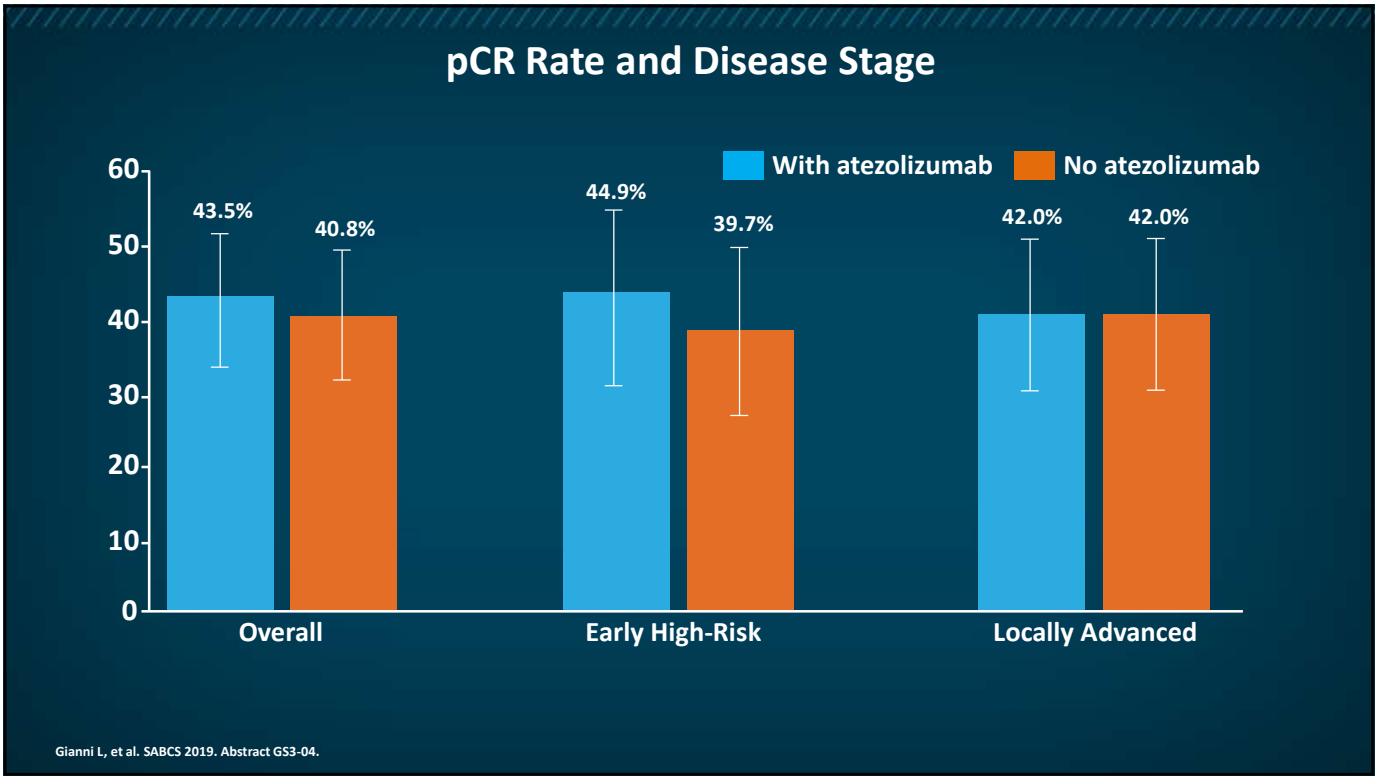
pCR Rate and Disease Stage
With atezolizumab
No atezolizumab
60
50
40
30
20
10
0
43.5%
40.8%
44.9%
39.7%
42.0%
42.0%
Overall
Early High-Risk
Locally Advanced
Gianni L, et al. SABCS 2019. Abstract GS3-04.

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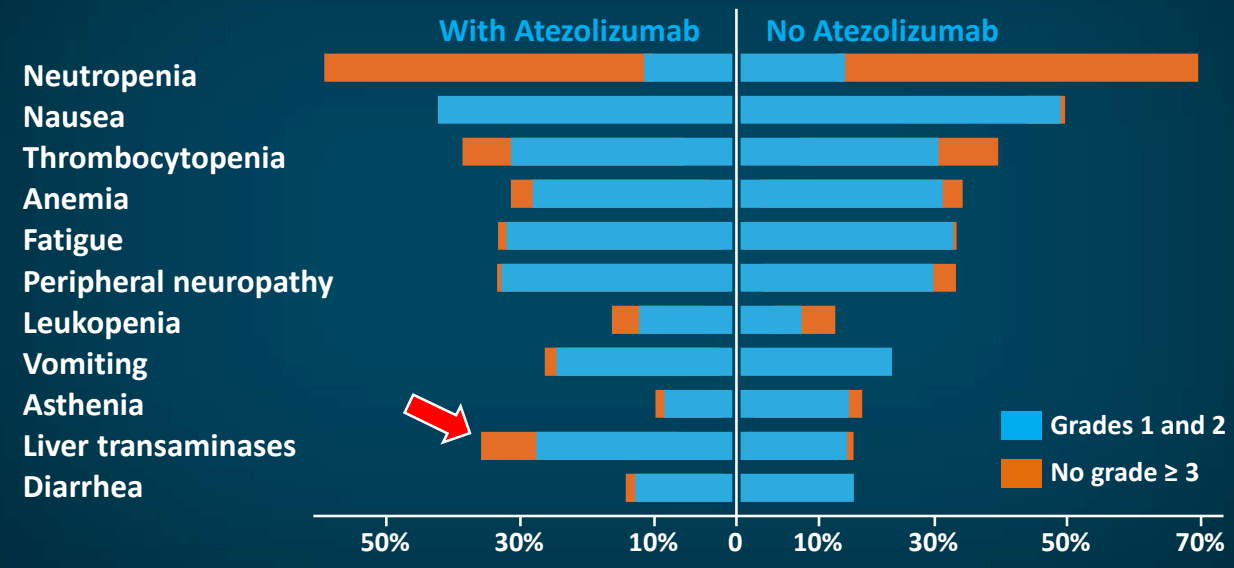
Treatment-Related Adverse Events (Incidence ≥ 15%)



Gianni L, et al. SABCS 2019. Abstract GS3-04.

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NeoTRIPaPDL1: Summary

- The addition of atezolizumab to neoadjuvant chemotherapy resulted in slightly higher rates of pCR when compared with neoadjuvant chemotherapy alone in the ITT population (43.5% vs 40.8%); however, the increase was not statistically significant
- Among patients whose tumors tested positive for PD-L1, 51.9% of patients in the atezolizumab + chemotherapy arm had pCR compared with 48.0% in the chemotherapy-only arm
- PD-L1 does not predict who benefits from adding checkpoint inhibitor

Gianni L, et al. SABCS 2019. Abstract GS3-04.

40

Summary of Key Immuno-oncology Trials in TNBC

Setting	Study Name	Study Treatment		Outcome: ITT
Neoadjuvant	KEYNOTE-522[1]	Paclitaxel + carboplatin AC/EC → Pembrolizumab/placebo (29 weeks) → Surgery → Pembrolizumab/placebo (24 weeks)		✓ pCR 64.8% with pembrolizumab vs 51.2%
	NeoTRIPaPDL1[2]	*Nab*-paclitaxel + carboplatin → AC/EC/FEC (12 weeks) → Surgery → Atezolizumab/placebo (24 weeks)		pCR 43.5% with atezolizumab vs 40.8%
1L metastatic	IMpassion 130[3,†]	*Nab*-paclitaxel ± atezolizumab		PFS: HR = 0.80, *P* = .0021
	KEYNOTE-355[4]	Pembrolizumab vs *nab*-paclitaxel/ paclitaxel/carboplatin + gemcitabine		PFS: HR = 0.82 (0.69-0.97)
2L-3L metastatic	KEYNOTE-119[5]	Pembrolizumab vs capecitabine/ eribulin/gemcitabine/vinorelbine		No significant improvement in OS with pembrolizumab

AC = doxorubicin and cyclophosphamide; EC = epirubicin and cyclophosphamide; FEC = fluorouracil, epirubicin, and cyclophosphamide.

1. Schmid P, et al. ESMO 2019. Abstract LBA8_PR. 2. Gianni L, et al. SABCS 2019. Abstract GS3-04. 3. Schmid P, et al. *N Engl J Med*. 2018;379:2108-2121. 4. Cortes J, et al. ASCO 2020. Abstract 1000. 5. Cortes J, et al. ESMO 2019. Abstract LBA21. Hamilton E. ASCO 2020.

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Immunotherapy Side Effects

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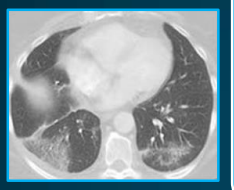
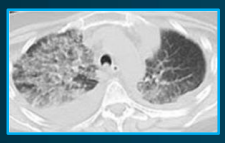
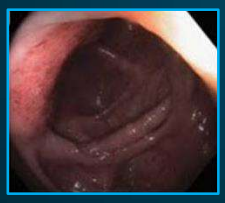
Immune-Related Adverse Event Spectrum





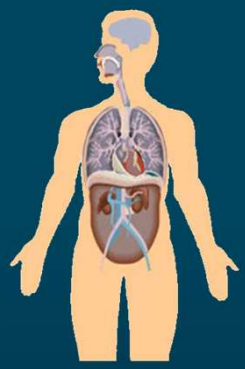


Endocrine
Thyroiditis
Hypothyroidism
Hyperthyroidism
Hypophysitis
Hypopituitarism
Adrenal insufficiency

Pulmonary
Pneumonitis
Respiratory failure

Gastrointestinal
Nausea, emesis
diarrhea, colitis,
perforation;
Pancreatitis

Neurologic
Neuropathy
Meningitis
Guillain-Barre syndrome



Fatigue
Anorexia
Nausea

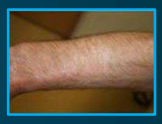
Ocular
Iritis
Uveitis
Conjunctivitis

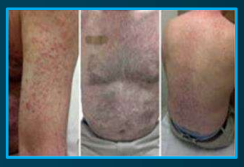
Cardiac
Pericarditis

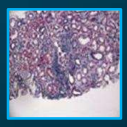
Dermatologic
Mucositis
Rash, vitiligo

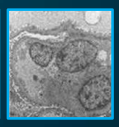
Hepatic
Transaminitis
Hepatitis

Renal
Nephritis
Renal insufficiency









Herbst R, et al. IASLC 2015. Borghaei H. ASCO 2017.

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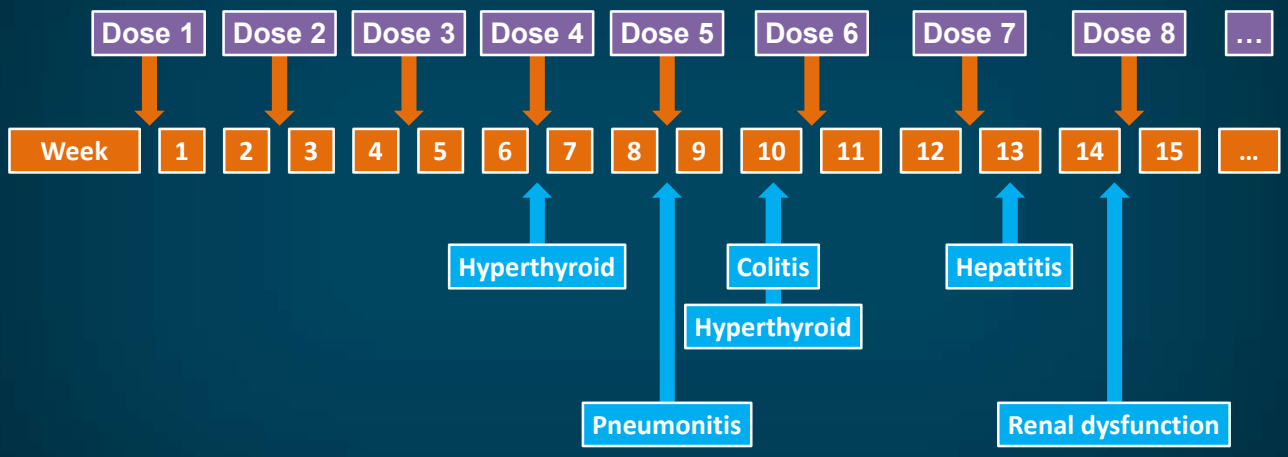
Median Time to Appearance of Immune-Related Adverse Events



Villadolid J, Amin A. *Transl Lung Cancer Res.* 2015;4:560-575.

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Immune-Related Adverse Events: Grading and Management Principles

Severity—CTCAE Grade	Ambulatory vs Inpatient Care	Corticosteroids	Other Immunosuppressive Drugs	Immunotherapy
1 ***Mild***	Ambulatory	Not recommended	Not recommended	Continue with close monitoring *(exception neurologic/some hematologic and cardiac toxicities)*
2 ***Moderate***	Ambulatory	Topical steroids *or* systemic steroids oral (low-dose) 0.5-1 mg/kg/d	Not recommended	Suspend temporarily* until symptoms and/or laboratory values revert to grade 1 levels or lower
3 ***Severe***	Hospitalization	**Systemic steroids (high-dose)** Oral *or* IV 1-2 mg/kg/d x 3 days, then reduce to 1 mg/kg/d; long taper (≥1 month)	To be considered for unresolved symptoms after 3-5 days of steroids Organ specialist referral advised	Suspend and discuss resumption based on risk/benefit ratio with patient
4 ***Very severe***	Hospitalization; *consider intensive care unit*	**Systemic steroids (high dose)** IV methylprednisolone 1-2 mg/kg/d x 3 days, then reduce to 1 mg/kg/d; long taper (≥1 month)	To be considered for unresolved symptoms after 3-5 days of steroids Organ specialist referral advised	Discontinue ***permanently***
5 ***Death***				

Some dysimmune toxicities may follow a specific management; this must be discussed with the organ specialist.

*In the case of skin or endocrine disorders, immunotherapy can be maintained.

CTCAE = Common Terminology Criteria for Adverse Events.

Champiat S, et al. *Ann Oncol*. 2016;27:559-574. Brahmer JR, et al. *J Clin Oncol*. 2018;36:1714-1768.

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NCCN Guidelines Version 1.2020

Management of Immune Checkpoint Inhibitor-Related Toxicities: DERMATOLOGIC

DERMATOLOGIC AEs

Maculopapular rash

ASSESSMENT/ GRADING

- Total body skin examination, including mucosa
- Assess for history of prior inflammatory dermatologic diseases
- Consider biopsy if unusual features

MANAGEMENT

Mild (grade 1)*
- Continue immunotherapy
- Topical emollient
- Oral antihistamine for pruritus
- Treatment with moderate potency topical steroids to affected areas

Moderate (grade 2)†
- Continue immunotherapy
- Topical emollient
- Oral antihistamine for pruritus
- Treatment with moderate-to-high potency topical steroids to affected areas

AND/OR
- Prednisone 0.5-1 mg/kg/d

Severe (grade 3-4)‡
- Hold immunotherapy
- Treatment with high potency topical steroids to affected areas
- Prednisone 0.5-1 mg/kg/d (increase dose up to 2 mg/kg/d if no improvement)
- Urgent dermatology consultation, consider biopsy
- Consider inpatient care

Macules/papules covering *< 10% BSA with or without symptoms (eg, pruritus, burning, tightness), †10%-30% BSA with or without symptoms (eg, pruritus, burning, tightness) and limiting instrumental ADLs, ‡> 30% BSA with or without associated symptoms and limiting self-care ADLs.

ADL = activities of daily living; BSA = body surface area.

NCCN practice guidelines. Management of immunotherapy-related toxicities. V1.2020 (https://www.nccn.org/professionals/physician_gls/pdf/immunotherapy.pdf). Accessed September 6, 2020.

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GI Adverse Event Management Algorithm

Rule out non-inflammatory causes. If non-inflammatory cause is identified, treat accordingly and continue IO therapy. Opiates/narcotics may mask symptoms of perforation. Infliximab should not be used in cases of perforation or sepsis.

Grade of Diarrhea/Colitis (NCI CTCAE v4)	Management	Follow-up
Grade 1 Diarrhea: < 4 stools/d over baseline Colitis: asymptomatic	• Continue IO therapy per protocol • Symptomatic treatment	• Close monitoring for worsening symptoms • Educate patient to report worsening immediately If worsens: • Treat as grade 2 or 3/4
Grade 2 Diarrhea: 4-6 stools/d over baseline; IV fluids indicated < 24 h; not interfering with ADL Colitis: abdominal pain; blood in stool	• Delay IO therapy per protocol • Symptomatic treatment	If improves to grade 1: • Resume IO therapy per protocol. If persists > 5-7 days or recurs: • 0.5-1 mg/kg/d methylprednisolone or oral equivalent • When symptoms improve to grade 1, taper steroids over ≥ 1 mo, consider prophylactic antibiotics for opportunistic infections, and resume IO therapy per protocol If worsens or persists > 3-5 days with oral steroids: • Treat as grade 3/4
Grade 3-4 Diarrhea (grade 3): ≥ 7 stools/d over baseline: incontinence; IV fluids ≥ 24 h; interfering with ADLs Colitis (grade 3): severe abdominal pain, medical intervention indicated, peritoneal signs Grade 4: life-threatening, perforation	• Discontinue IO therapy per protocol • 1-2 mg/kg/d methylprednisolone IV or IV equivalent • Add prophylactic antibiotics for opportunistic infections • Consider lower endoscopy	If improves: • Continue steroids until grade 1, then taper over ≥ 1 mo If persists > 3-5 days or recurs after improvement: • Add infliximab 5 mg/kg (if no contraindication). Note: Infliximab should not be used in cases of perforation or sepsis

GI = gastrointestinal; IO = immuno-oncology; NCI = National Cancer Institute.

Brahmer JR, et al. *J Clin Oncol*. 2018;36:1714-1768. Borghaei H. ASCO 2017.

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NCCN Guidelines Version 1.2020

Management of Immune Checkpoint Inhibitor-Related Toxicities: HEPATIC

HEPATIC AEs	ASSESSMENT/GRADING	MANAGEMENT
Transaminitis without elevated bilirubin	• Rule out viral etiology, disease-related hepatic dysfunction, other drug-induced transaminase elevations • Consider GI evaluation • Ultrasound – Consider magnetic resonance cholangiopancreatography if normal ultrasound • Limit/discontinue hepatotoxic medications (assess acetaminophen, dietary supplement, and alcohol use)	**Mild (grade 1) < 3 x ULN** • Continue immunotherapy, consider holding immunotherapy for concerning laboratory value trend • Assess transaminases and bilirubin with increased frequency **Moderate (grade 2) 3-5 x ULN** • Hold immunotherapy • Monitor liver function tests every 3-5 days • Consider prednisone 0.5-1 mg/kg/d **Severe (grade 3) > 5-20 x ULN** • Permanently discontinue immunotherapy • Initiate prednisone 1-2 mg/kg/d • Consider inpatient care • Monitor liver enzymes every 1-2 days • Hepatology consultation • If steroid refractory or no improvement after 3 days, consider adding mycophenolate • Infliximab should not be used for hepatitis **Life-threatening (grade 4) > 20 x ULN** • Permanently discontinue immunotherapy • Initiate prednisone/methylprednisolone 2 mg/kg/d • Inpatient care • Monitor liver enzymes daily • Hepatology consultation • Liver biopsy if no contraindications • If steroid refractory or no improvement after 3 days, consider adding mycophenolate • Infliximab should not be used for hepatitis
Grade > 1 transaminitis with bilirubin > 1.5x ULN (unless Gilbert's syndrome)	See ICI GI-4	

ULN = upper limit of normal.

NCCN practice guidelines. Management of immunotherapy-related toxicities. V1.2020 (https://www.nccn.org/professionals/physician_gls/pdf/immunotherapy.pdf). Accessed September 6, 2020.

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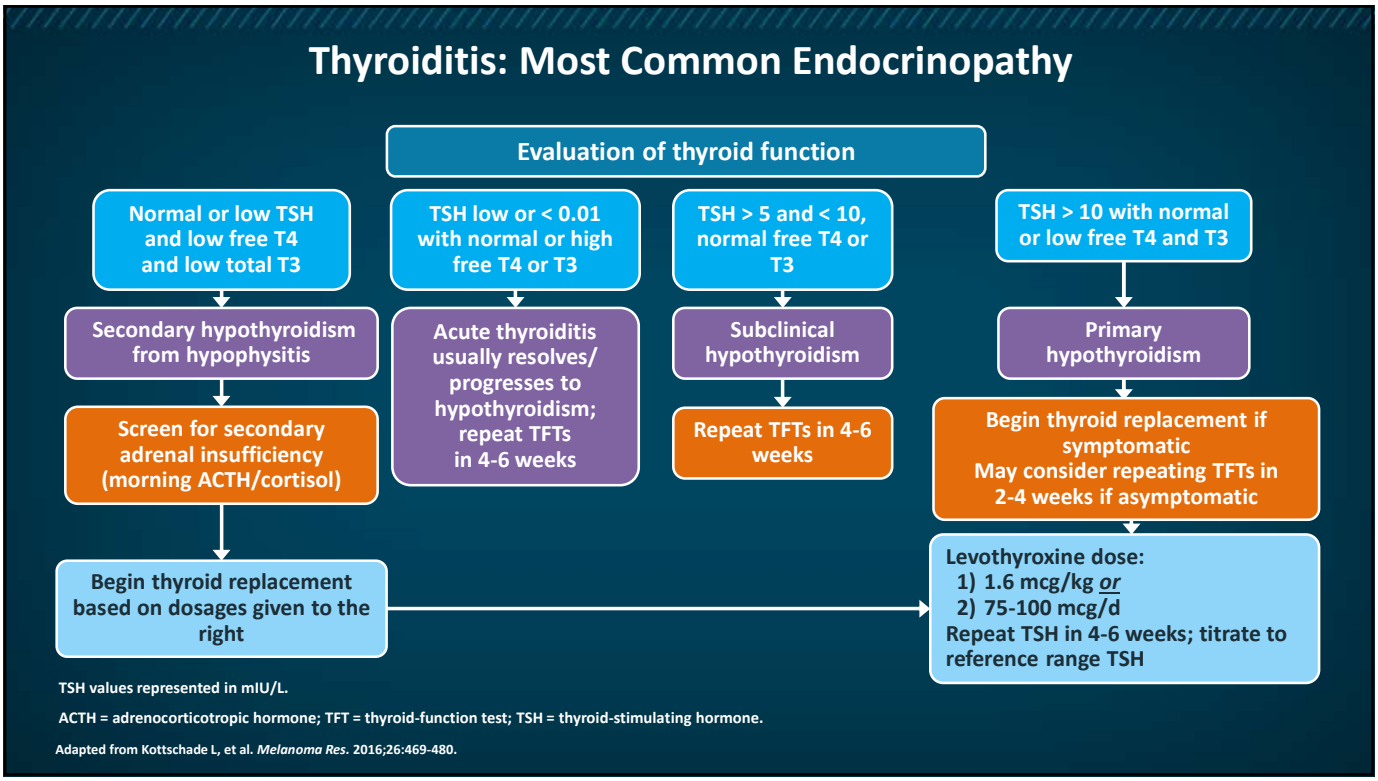
Thyroiditis: Most Common Endocrinopathy
Evaluation of thyroid function
Normal or low TSH and low free T4 and low total T3
TSH low or < 0.01 with normal or high free T4 or T3
TSH > 5 and < 10, normal free T4 or T3
TSH > 10 with normal or low free T4 and T3
Secondary hypothyroidism from hypophysitis
Acute thyroiditis usually resolves/ progresses to hypothyroidism; repeat TFTs in 4-6 weeks
Subclinical hypothyroidism
Primary hypothyroidism
Screen for secondary adrenal insufficiency (morning ACTH/cortisol)
Repeat TFTs in 4-6 weeks
Begin thyroid replacement if symptomatic
May consider repeating TFTs in 2-4 weeks if asymptomatic
Begin thyroid replacement based on dosages given to the right
Levothyroxine dose:
1) 1.6 mcg/kg or
2) 75-100 mcg/d
Repeat TSH in 4-6 weeks; titrate to reference range TSH
TSH values represented in mIU/L.
ACTH = adrenocorticotropic hormone; TFT = thyroid-function test; TSH = thyroid-stimulating hormone.
Adapted from Kottschade L, et al. Melanoma Res. 2016;26:469-480.

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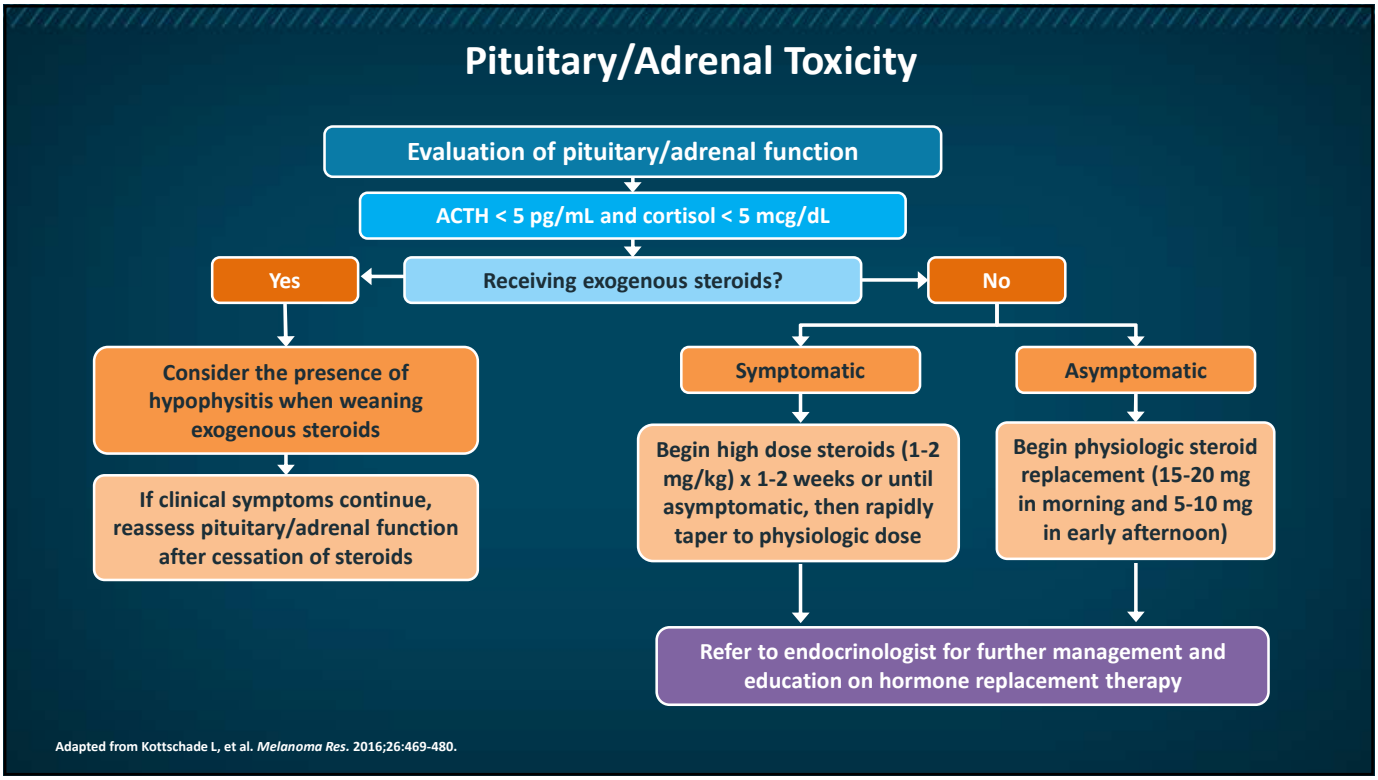
Pituitary/Adrenal Toxicity
Evaluation of pituitary/adrenal function
ACTH < 5 pg/mL and cortisol < 5 mcg/dL
Receiving exogenous steroids?
Yes
No
Consider the presence of hypophysitis when weaning exogenous steroids
If clinical symptoms continue, reassess pituitary/adrenal function after cessation of steroids
Symptomatic
Asymptomatic
Begin high dose steroids (1-2 mg/kg) x 1-2 weeks or until asymptomatic, then rapidly taper to physiologic dose
Begin physiologic steroid replacement (15-20 mg in morning and 5-10 mg in early afternoon)
Refer to endocrinologist for further management and education on hormone replacement therapy
Adapted from Kottschade L, et al. Melanoma Res. 2016;26:469-480.

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Pulmonary Adverse Event Management Algorithm

Rule out non-inflammatory causes. If non-inflammatory cause, treat accordingly and continue IO therapy. Evaluate with imaging and pulmonary consultation.

Grade of Pneumonitis (NCI CTCAE v4)	Management	Follow-up
Grade 1 Radiographic changes only	• Consider delay of IO therapy • Monitor for symptoms every 2-3 days • Consider pulmonary and ID consults	• Re-image at least Q3W If worsens: • Treat as grade 2 or 3-4
Grade 2 Mild-to-moderate new symptoms	• Delay IO therapy per protocol • Pulmonary and ID consults • Monitor symptoms daily; consider hospitalization • 1-mg/kg/d methylprednisolone IV or oral equivalent • Consider bronchoscopy, lung biopsy	• Re-image every 1-3 days If improves: • When symptoms return to near baseline, taper steroids over ≥ 1 month and then resume IO therapy per protocol and consider prophylactic antibiotics If not improving after 2 weeks or worsening: • Treat as grade 3-4
Grade 3-4 Severe new symptoms; new/worsening hypoxia; life-threatening	• Discontinue IO therapy per protocol • Hospitalize • Pulmonary and ID consults • 2-4 mg/kg/d methylprednisolone IV or IV equivalent • Add prophylactic antibiotics for opportunistic infections • Consider bronchoscopy, lung biopsy	If improves to baseline: • Taper steroids over ≥ 6 weeks If not improving after 48 hours or worsening: • Add additional immunosuppression (eg, infliximab, cyclophosphamide, IV immunoglobulin, or mycophenolate mofetil)

ID = infectious disease.

Brahmer JR, et al. *J Clin Oncol*. 2018;36:1714-1768. Borghaei H. ASCO 2017.

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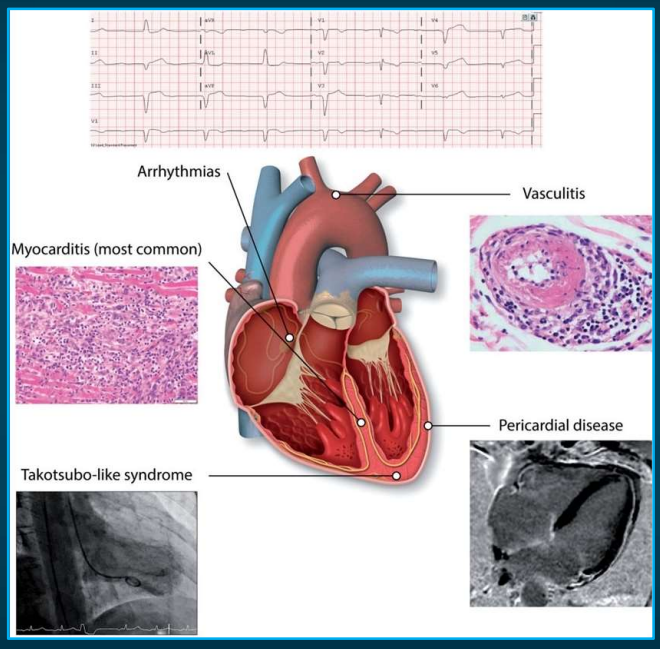
Immune Checkpoint Inhibitor–Associated Cardiovascular Toxicities



Hu JR, et al. *Cardiovasc Res*. 2019;115:854-868.

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Case Study 1: Question 1

Sandra B is a 54-year-old postmenopausal woman who was diagnosed with early stage invasive ductal carcinoma of the right breast 2 years ago with a 3-cm lesion and no nodal involvement, triple-negative, high-grade histology, BRCA1- and BRCA2-negative. She declined neoadjuvant chemotherapy, underwent bilateral mastectomy, received adjuvant chemotherapy and no radiation, and had minimal side effects. She remained without disease free for 23 months and presented with right hip pain, weight loss, and fatigue. Imaging studies showed a 2-cm right acetabular lesion, iliac and sacral metastasis, besides lung nodules and liver lesion. Brain MRI was negative. Biopsy of the lung lesion confirmed mTNBC, and PD-L1 was positive with SP-142 antibody.

What is the most appropriate treatment option for this patient?

A. Capecitabine

B. Carboplatin and gemcitabine

C. Atezolizumab and *nab*-paclitaxel

D. Paclitaxel

MRI = magnetic resonance imaging.

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Case Study 1: Question 2

The patient receives atezolizumab and *nab*-paclitaxel. After 3 months of therapy, she presents with anorexia, vomiting, abdominal pain, weakness, lethargy, and intermittent fever. Laboratory findings showed hyponatremia, low blood sugars, low morning cortisol levels, and elevated ACTH. She is diagnosed with primary adrenal insufficiency as an adverse effect of immunotherapy.

You manage this patient with all of the following *except*:

A. Reduce the dose and continue with immunotherapy

B. Request an endocrine consultation

C. Add prednisone **or** hydrocortisone and titrate the doses based on symptoms

D. Obtain an MRI of the brain

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Case Study 2

Katie B is a 60-year-old postmenopausal woman who is diagnosed with stage III TNBC and is on pembrolizumab + chemotherapy on a clinical trial. She has no past medical history. After 4 cycles of therapy, she presents with worsening shortness of breath on exertion and a dry, nonproductive cough. She denies any fevers or chills or recent sick contacts. She has a drop in oxygen level to 94% at walking; however at rest, she is breathing comfortably and fully conversant.

What is the most appropriate next step in management?

A. Hold chemoimmunotherapy and emergently initiate corticosteroids for immune-related pneumonitis

B. Hold chemoimmunotherapy, obtain a chest CT, and consider additional workup for immune-related pneumonitis

C. Continue chemoimmunotherapy treatment and refer the patient to a pulmonary specialist for further workup and management

D. Hold chemoimmunotherapy and begin oral antibiotics for bacterial pneumonia

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The Multidisciplinary Oncology Team

Optimizing Patient Care and Survivorship Through Shared Decision-Making

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Role of Oncology Nursing in IO Management

- Nurses should be aware of the mechanisms of immunotherapy and safe administration, which is different from that of cytotoxic agents
- Immunotherapy is often given in combination with chemotherapy or during radiation; dose reduction is not necessary
- Onset of immune-related AEs occurs later than the infusion time; nurses should be well versed and assess and monitor for possible immune-related AEs
- Nurses should educate patients about side effects of IO and encourage them to be engaged in informing them of the side effects
- Safety standards set by ASCO and Oncology Nursing Society guidelines should be the basis for policies and procedures for IO administration

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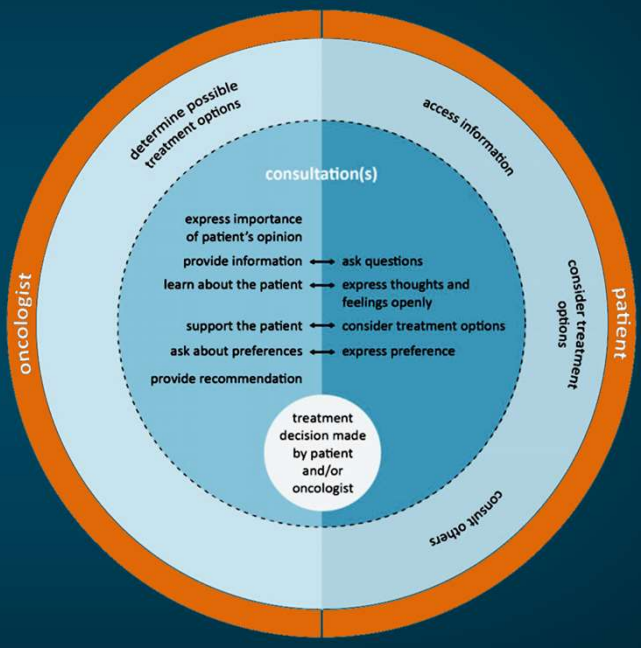
Shared Decision-Making in Oncology: What Is It?

- A dynamic process in which both patients and oncologists have complimentary roles during and outside the medical encounter
- Patients play an active role
- SDM should not be imposed on patients, but encouraged through supportive means



SDM = shared decision-making.

Bomhof-Roordink H, et al. *Psycho-Oncology.* 2019;28:139-146.

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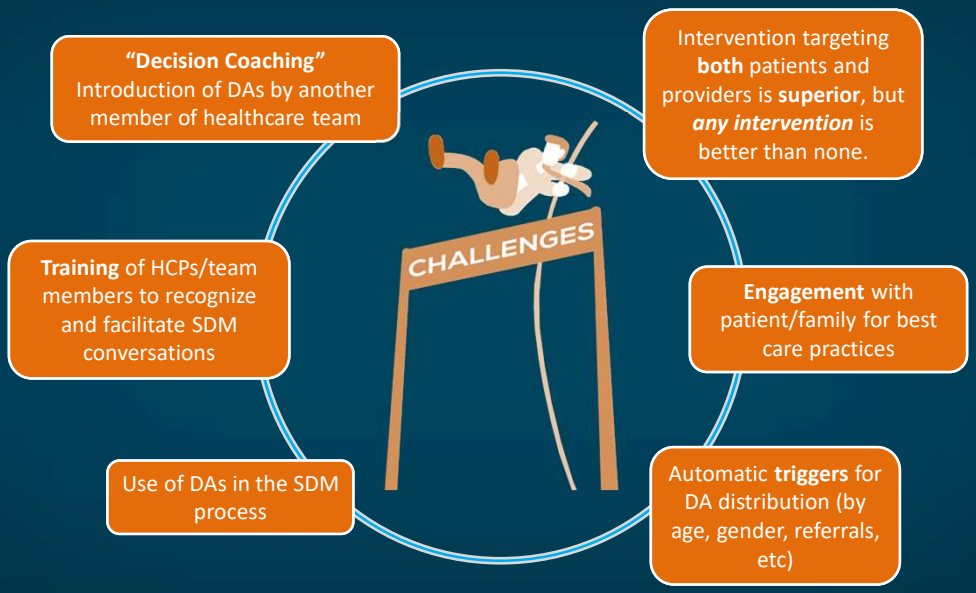
Overcoming Barriers



DA = decision aids; HCP = health care provider.

Agency for Healthcare Research and Quality 2015 (www.ahrq.gov/sites/default/files/wysiwyg/professionals/education/curriculum-tools/shareddecisionmaking/webinars/sharewebinar518-slides.pdf). Accessed September 8, 2020.

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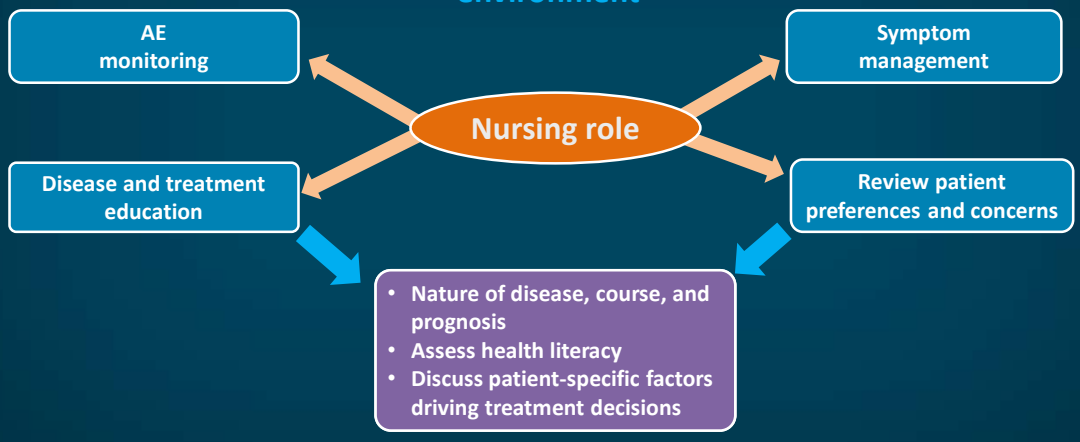
Role of the Oncology Nurse

Collaboration of Care

Bridging the gap between the patient and oncology through a team environment



Myers NM. *LPN2009.* 2009;5:18-23. Rieger PT, Yarbro CH. In: Kufe DW, et al. *Cancer Medicine.* 6th ed. Hamilton, ON: BC Decker; 2003.

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Summary

- TILs have prognostic and predictive value in the treatment of TNBC
- IMpassion 130 is the first phase 3 study to show immune checkpoint inhibition in combination with *nab*-paclitaxel has significant improvement in PFS and OS for patients with locally advanced or metastatic TNBC whose tumors express PD-L1
- KEYNOTE-355 trial also confirmed pembrolizumab + chemotherapy improved PFS compared with chemotherapy alone across all patent subgroups
- Neoadjuvant therapy with pembrolizumab + chemotherapy is associated with larger pCR benefit than chemotherapy alone in stage II and III TNBC, as shown in KEYNOTE-522
- All organs can be affected by IO therapies, risk factors are unknown, and high-dose steroids are the main stay of treatment for non-endocrine immune-related AEs, with infliximab for steroid-refractory cases

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Thank you!

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