Expert Insights on Triple-Negative Breast Cancer: Preparing for the Next Wave of Treatments

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Welcome and Introductions

Disclosures

- **Heather Greene, MSN, FNP, AOCNP®**
  - Speakers Bureau: Pfizer
- **Lee Schwartzberg, MD, FACP**
  - Consultant: Amgen, AstraZeneca, Genentech/Roche, Pfizer

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This activity may include discussion of agents that have not yet been approved by the U.S. Food and Drug Administration and investigational uses of approved products. Please consult prescribing information and practice guidelines for detail regarding safe and effective use of therapeutic agents.

Learning Objectives

- Evaluate the clinical significance of recent and emerging data regarding the efficacy and safety of approved therapeutic options for TNBC
- Develop strategies to identify and manage AEs associated with PARP inhibitors and ICIs used in patients with TNBC
- Identify novel therapeutic strategies being investigated for TNBC

AEs = adverse events; ICIs = immune checkpoint inhibitors; PARP = poly ADP ribose polymerase; TNBC = triple-negative breast cancer

TNBC: Pathophysiology and Molecular Classification

What Is Triple-Negative Breast Cancer?

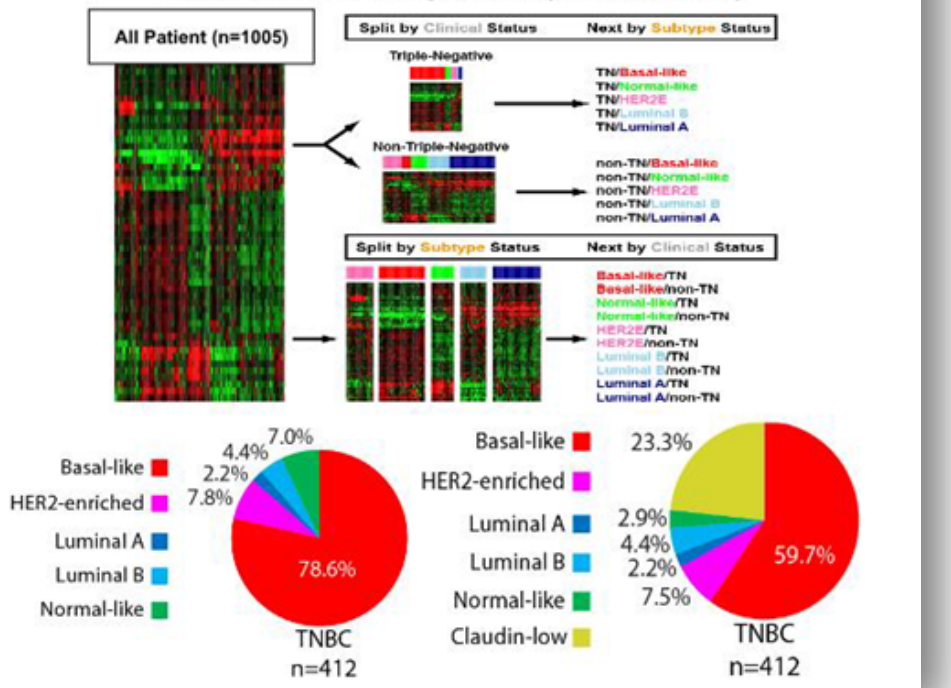
- Triple negative: ER negative, PR negative, HER2 negative
  - Depending on thresholds used to define ER and PR positivity and methods for HER2 testing
- TNBC accounts for 10% to 17% of all breast carcinomas
- Higher incidence in African Americans
- Significantly more aggressive than other molecular subtypes
- Majority grade 3 tumors
- Peak risk of recurrence at 1 to 3 years
- Increased mortality rate first 5 years
- Rapid progression from distant recurrence to death

ER = estrogen receptor; PR = progesterone receptor

Reis-Filho JS, et al. *Histopathology.* 2008;52:108-18; Dent R, et al. *Clin Cancer Res.* 2007;13:4429-34.

TNBC Can Be Classified Molecularly

Molecular Characterization of Basal-Like and Non-Basal-Like Triple-Negative Breast Cancers.
Prat et al., The Oncologist, 2013 (PMID:23404817)



Refinement of Triple-Negative Breast Cancer Molecular Subtypes: Implications for Neoadjuvant Chemotherapy Selection.
Lehmann, Jovanović, Chen, Estrada, Johnson, Shyr, Moses, Sanders, and Pietenpol.
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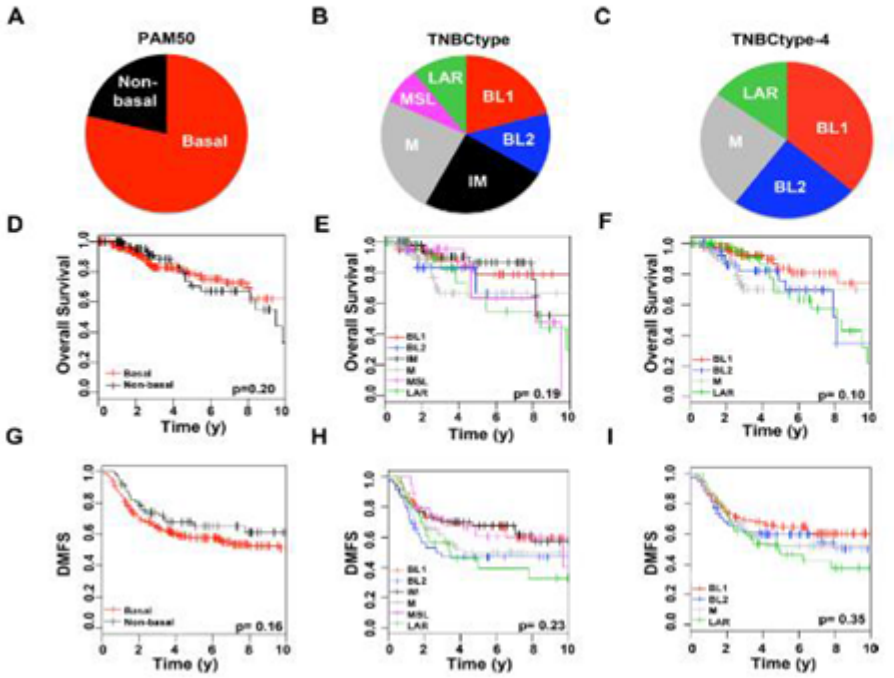

The updated TNBCtyper removes the Immunomodulatory Group, and the Mesenchymal Stem-Like Group.

"We used histopathological quantification and laser-capture microdissection to determine that transcripts in the previously described immunomodulatory (IM) and mesenchymal stem-like (MSL) subtypes were contributed from infiltrating lymphocytes and tumor-associated stromal cells, respectively. Therefore, we refined TNBC molecular subtypes from six (TNBCtype) into four (TNBCtype-4)".

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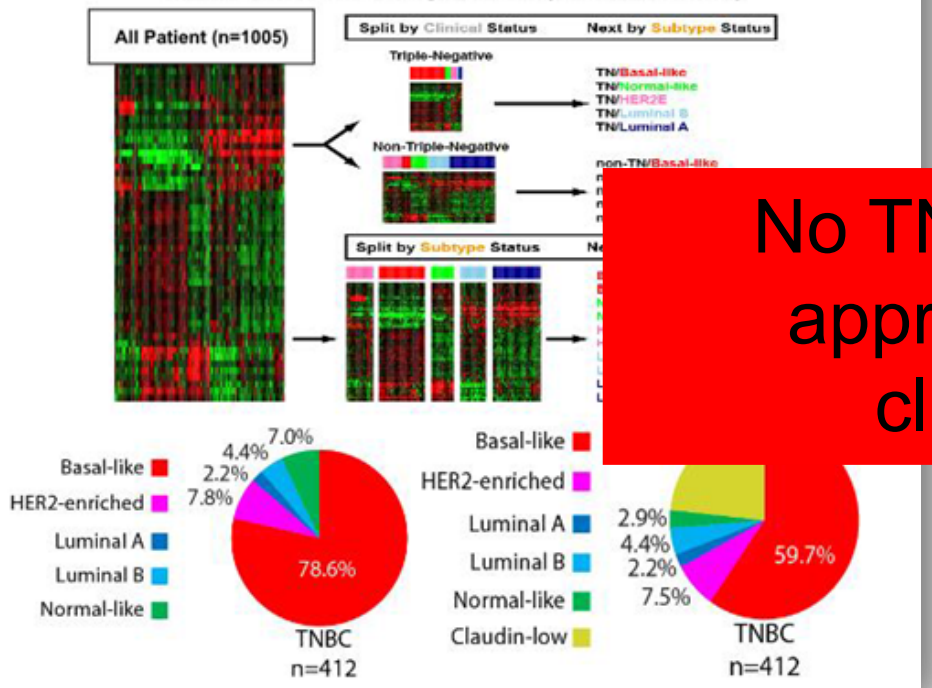

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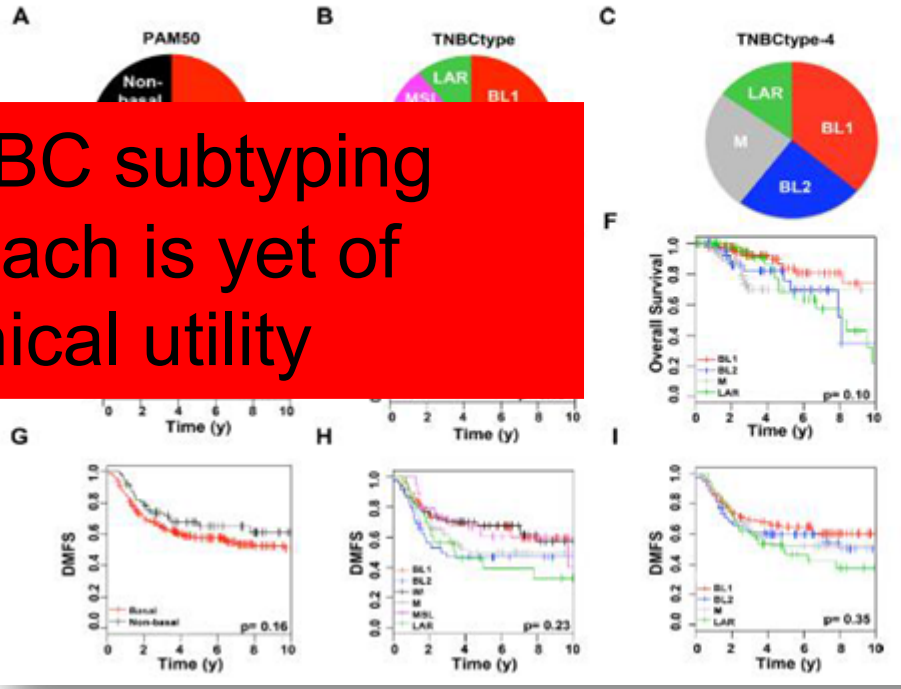

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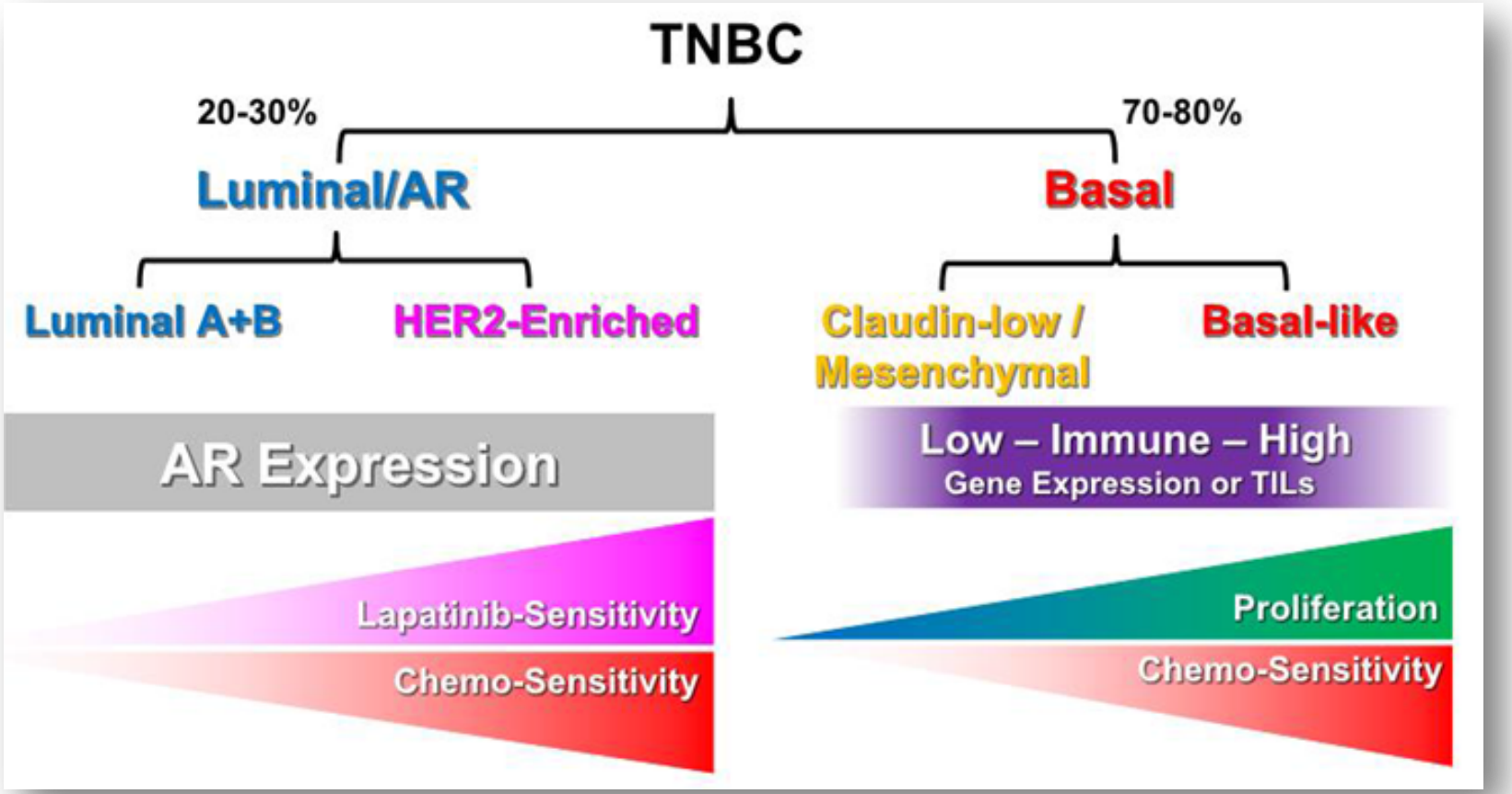
No TNBC subtyping approach is yet of clinical utility

Stratification of TNBC



AR = androgen receptor; TILs = tumor-infiltrating lymphocytes

Optimizing Current Standards of Care

Early-Stage Disease

Management of Early-Stage Disease

- Locoregional
  - Lumpectomy + radiation therapy preferred
    - No advantage for mastectomy; may result in inferior outcomes
  - Patients with germline mutations: mastectomy preferred (for reasons of secondary prophylaxis)
- Early-stage treatment
  - Alkylator + anthracycline + taxane-based chemotherapy for all patients
    - Exceptions made for small cancers or ineligible patients
  - Strongly consider neoadjuvant approach except for small cancers
  - Consider post-neoadjuvant chemotherapy with adjuvant capecitabine, based on residual disease burden at surgical excision
  - Consider platinum drugs if patient has a known *BRCA1/2* germline mutation

Treatment of ESBC-TNBC

- Neoadjuvant chemotherapy
  - Rationale
  - Benefit of pCR
  - Standard chemotherapy
  - Use of platin
  - Post-neoadjuvant cape (CREATE-X)
  - Pembrolizumab?
- Adjuvant therapy

ESBC = early-stage breast cancer; pCR = pathologic complete response

Neoadjuvant Chemotherapy for TNBC: Current Landscape

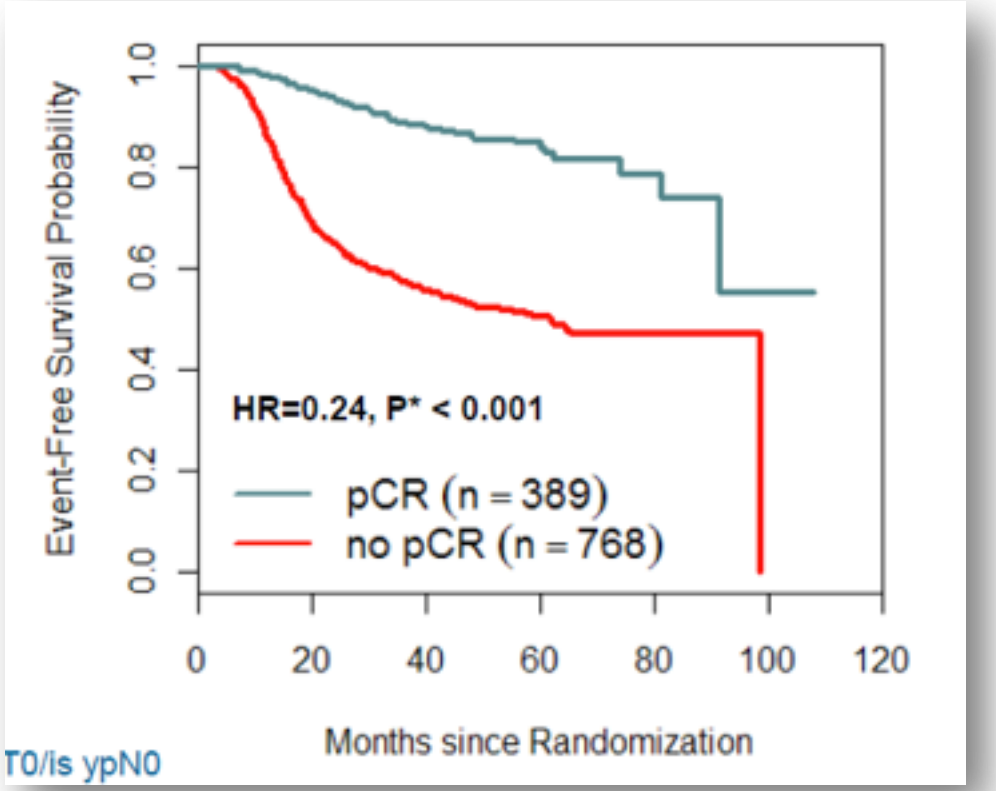
- Conventional sequential AC/T chemotherapy yields pCR in 30% to 42%
  - Additional ≅ 10-15% achieve near pCR (RCB 1)
- Addition of carboplatin to A/T chemotherapy improves pCR (54%-58%)
  - Increased toxicity, survival data pending
  - Robust response biomarkers not available
- Achievement of pCR is associated with excellent 3- to 5-year EFS/OS
  - Lack of pCR is associated with high recurrence risk
- Several genomic and molecular biomarkers of neoadjuvant chemotherapy response in TNBC have been retrospectively evaluated in GE signatures, TILs/immune markers, TNBC subtypes, tumor genomic scars, etc.

AC/T = doxorubicin, cyclophosphamide, and paclitaxel; A/T = doxorubicin and paclitaxel; EFS = event-free survival; GE = gene expression; OS = overall survival; RCB = residual cancer burden

Von Minckwitz G, et al. *Lancet Oncol.* 2014;15:747-56; Sikov WM, et al. *J Clin Oncol.* 2014;33:13-21; Rugo HS, et al. *N Engl J Med.* 2016;375:23-34; Alba E, et al. *Breast Cancer Res Treat.* 2012;136:487-93; Tamura K, et al. *J Clin Oncol.* 2014;32 (suppl; abstr 1017); Sharma P, et al. *Clin Cancer Res.* 2016;23:649-57; Loibl S, et al. *Lancet Oncol.* 2018;19:497-509; Symmans WF, et al. *J Clin Oncol.* 2017;35:1049-60; Cortazar P, et al. *Lancet.* 2014;384:164-72; Yee D, et al. 2017 SABCS oral presentation.

pCR as a Surrogate Endpoint in TNBC

- Neoadjuvant chemotherapy for TNBC
  - pCR (ypT0/is N0) rate: 34% (meta-analysis)
- CTNeoBC pooled analysis of 12 randomized trials:[1,2]
  - Of 1157 patients with TNBC
    - 33.6% achieved pCR
  - TNBC patients with pCR had
    - EFS HR 0.24
    - (95% CI, 0.18-0.33)
    - OS HR 0.16
    - (95% CI, 0.11-0.25)
    - Compared with non-pCRs



CI = confidence interval; HR = hazard ratio

1. Cortazar P, et al. *Cancer Res.* 2012;72(24 Suppl):S1-11; 2. Cortazar P, et al. *Lancet*. 2014;384:164-72.

I-SPY2 Neoadjuvant Trial

- Pembrolizumab graduated in all HER2- signatures, both HR+/HER2- and triple negative
- Neoadjuvant paclitaxel x 12 with/without pembrolizumab followed by AC x 4
- Adaptive randomization on I-SPY2

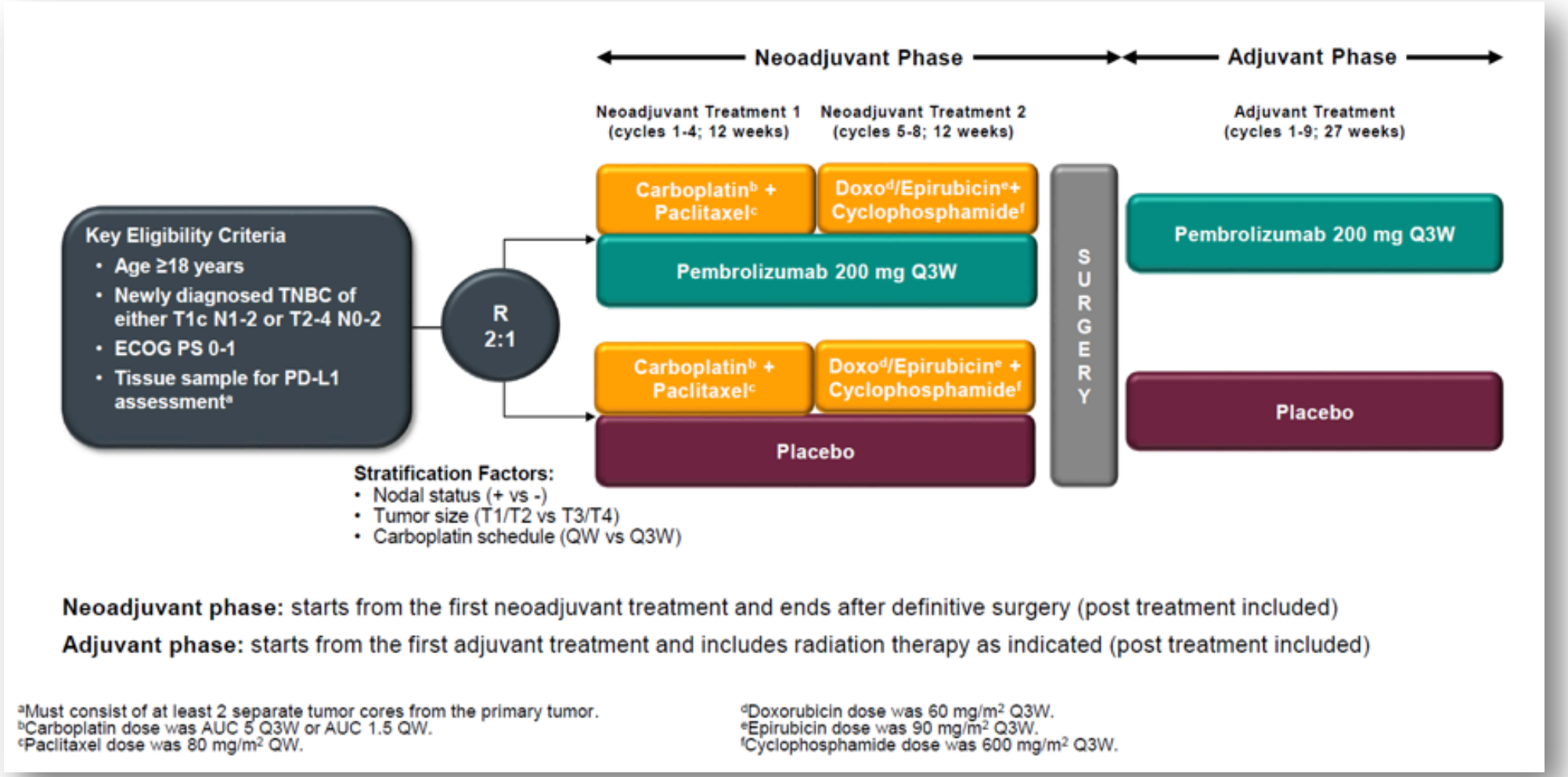
Signature	Estimated pCR rate (95% probabilty interval)		Probability pembro is superior to control	Predictive probability of success in phase 3
	Pembro	Control		
All HER2-	**0.46** (0.34 – 0.58)	**0.16** (0.06 – 0.27)	**> 99%**	**99%**
TNBC	**0.60** (0.43 – 0.78)	**0.20** (0.06 – 0.33)	**>99%**	**>99%**
HR+/HER2-	**0.34** (0.19 – 0.48)	**0.13** (0.03 – 0.24)	**>99%**	**88%**

The Bayesian model estimated pCR rates adjust to characteristics of the I-SPY2 population. The raw pCR rates are higher than the model estimate of 0-604 in TNBC.

AC = doxorubicin and cyclophosphamide

Nanda R, et al. *J Clin Oncol.* 2017;35 (suppl; abstr 506).

KEYNOTE-522 Study Design



Neoadjuvant phase: starts from the first neoadjuvant treatment and ends after definitive surgery (post treatment included)

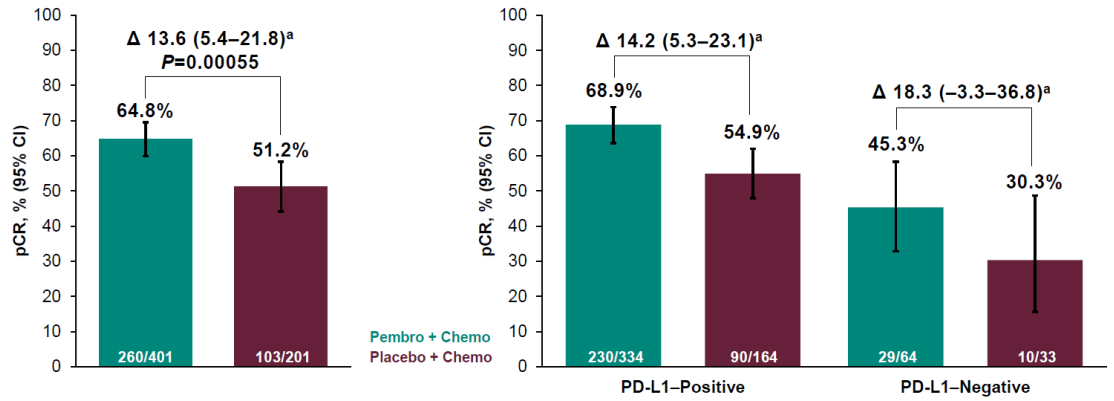
Adjuvant phase: starts from the first adjuvant treatment and includes radiation therapy as indicated (post treatment included)

[a]Must consist of at least 2 separate tumor cores from the primary tumor.
[b]Carboplatin dose was AUC 5 Q3W or AUC 1.5 QW.
[c]Paclitaxel dose was 80 mg/m^2 QW.
[d]Doxorubicin dose was 60 mg/m^2 Q3W.
[e]Epirubicin dose was 90 mg/m^2 Q3W.
[f]Cyclophosphamide dose was 600 mg/m^2 Q3W.

Schmid P, et al. ESMO 2019. Abstract LBA8_PR

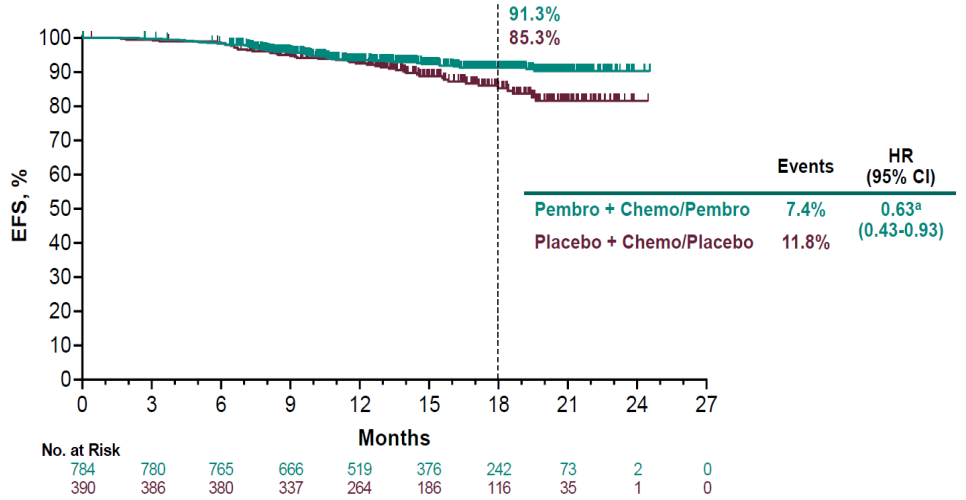
KEYNOTE-522

Pathological Complete Response at IA1



[a]Estimated treatment difference based on Miettinen & Nurminen method stratified by randomization stratification factors. [b]PD-L1 assessed at a central laboratory using the PD-L1 IHC 22C3 pharmDx assay and measured using the combined positive score (CPS; number of PD-L1–positive tumor cells, lymphocytes, and macrophages divided by total number of tumor cells x 100); PD-L1–positive = CPS ≥1. Data cutoff date: September 24, 2018.

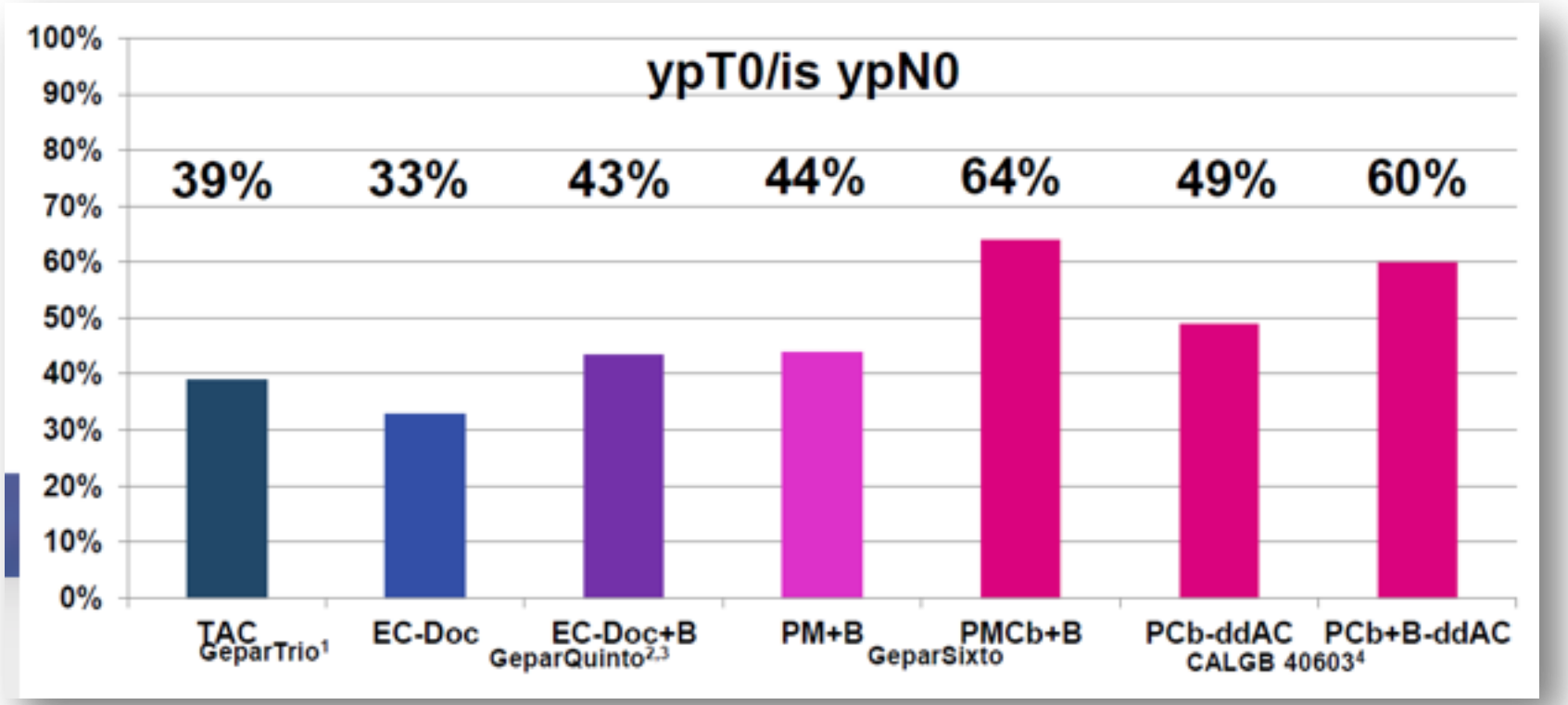
Event-Free Survival at IA2



[a]Prespecified *P* value boundary of 0.000051 not reached at this analysis (the first interim analysis of EFS).
Hazard ratio (CI) analyzed based on a Cox regression model with treatment as a covariate stratified by the randomization stratification factors. Data cutoff April 24, 2019.

Schmid P, et al. ESMO 2019. Abstract LBA8_PR

pCR Has Increased in TNBC With NACT Evolution



NACT = neoadjuvant chemotherapy

1. Huober J, et al. *Breast Cancer Res Treat.* 2010;124:133-40; 2. von Minckwitz G, et al. *N Engl J Med.* 2012;366(4):299-309; 3. Gerber B, et al. *Ann Oncol.* 2013;24:2978-84; 4. Sikov W, et al. SABCS 2013. Abstract S5-01.

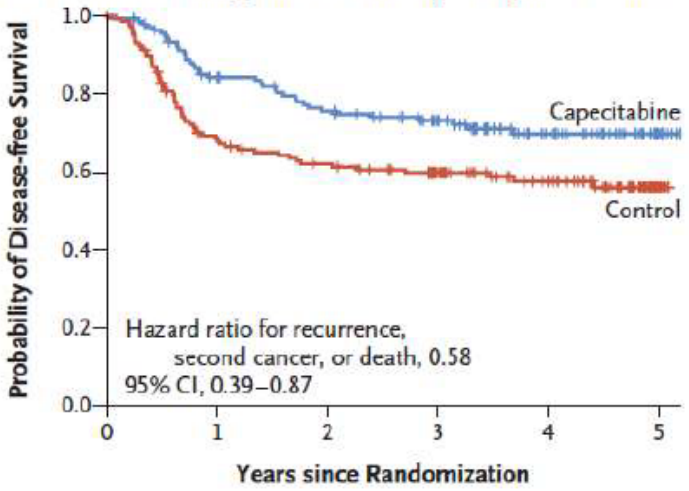
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Adjuvant Capecitabine for Breast Cancer after Preoperative Chemotherapy

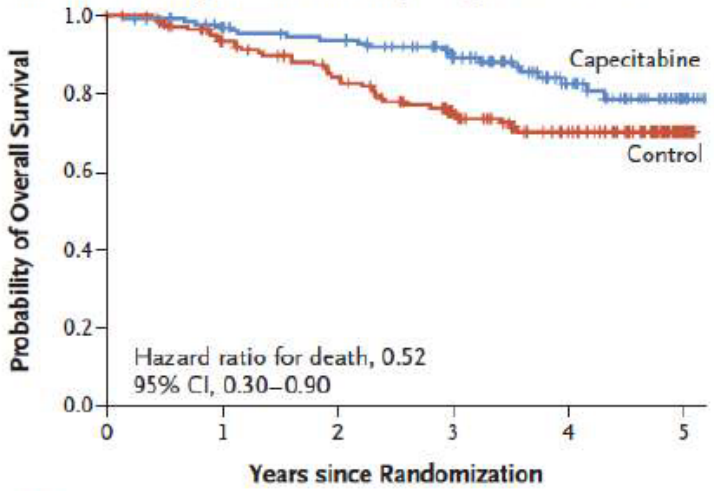
N. Masuda, S.-J. Lee, S. Ohtani, Y.-H. Im, E.-S. Lee, I. Yokota, K. Kuroi, S.-A. Im, B.-W. Park, S.-B. Kim, Y. Yanagita, S. Ohno, S. Takao, K. Aogi, H. Iwata, J. Jeong, A. Kim, K.-H. Park, H. Sasano, Y. Ohashi, and M. Toi

C **Disease-free Survival among Patients with Triple-Negative Disease**



No. at Risk						
Capecitabine	139	109	96	76	42	11
Control	147	95	84	69	47	6

D **Overall Survival among Patients with Triple-Negative Disease**



No. at Risk						
Capecitabine	139	124	116	91	50	11
Control	147	125	108	82	52	9

Masuda N, et al. *N Engl J Med.* 2017;376:2147-2159.

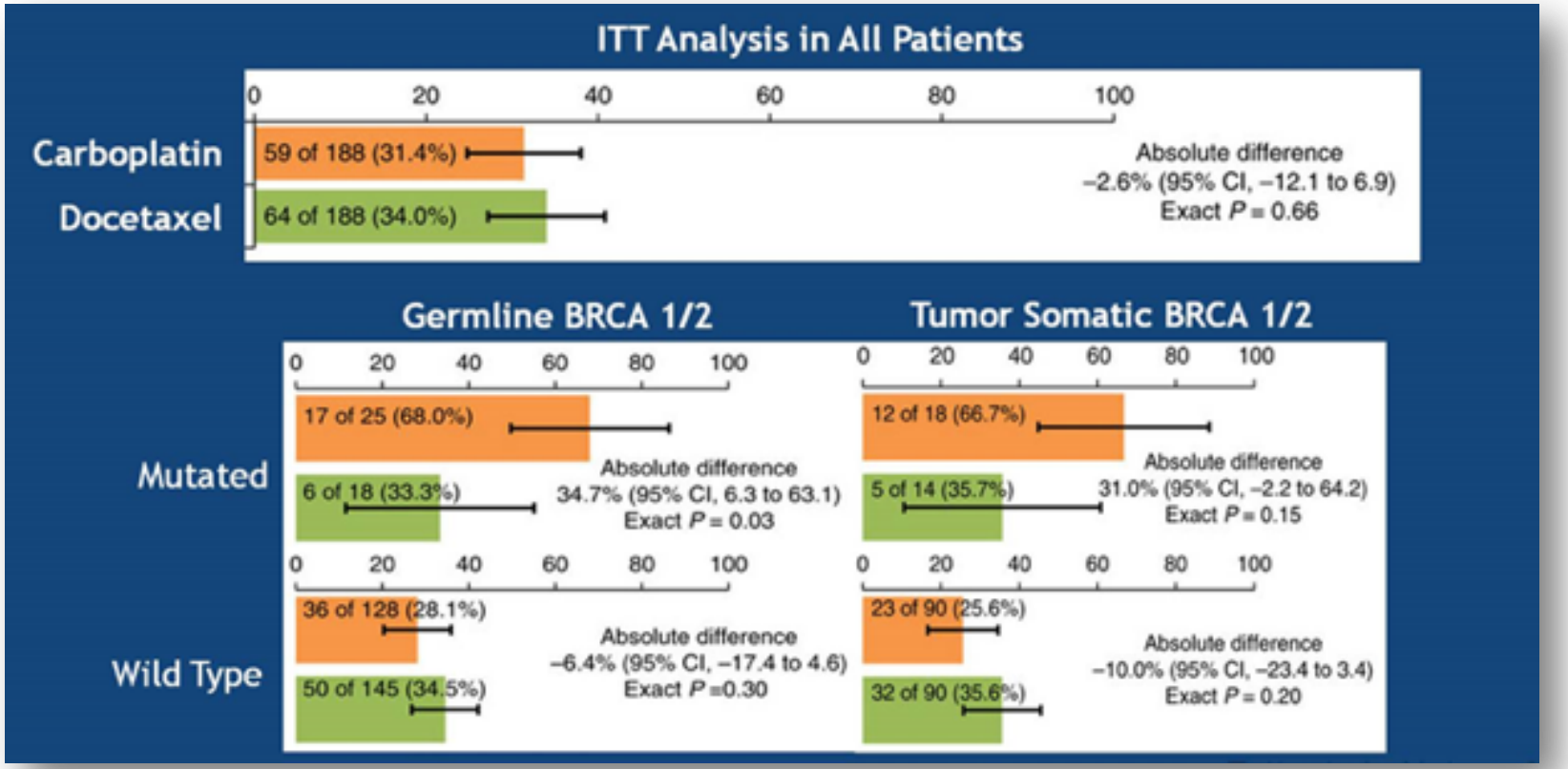
Advanced TNBC

Advanced TNBC: Current Standard of Care

- Heterogeneous group of cancers
- Poor prognosis: median OS 12-18 months
- Workup
  - Test for germline *BRCA* mutations
  - Test for PD-L1
  - Consider CNS screening
- Treatment
  - Germline *BRCA1/2*-mutated subgroup
    - Olaparib
    - Talazoparib
    - Platinum
  - Taxane first line (TNT trial)
  - Single agent unless high tumor burden

CNS = central nervous system

TNT Trial: First-Line Carboplatin vs. Docetaxel



ITT = intent to treat

Tutt A, et al. *Nat Med.* 2018;24:628-37.

Chemotherapy for Advanced TNBC Has Modest Activity

Drug	Phase	N	Population	ORR, %	PFS, months	OS, months	Source
1st-line treatment							
Carboplatin	III	188	1st line	31	3.1	12.4	Tutt A, SABCS 2014
Docetaxel	III	188	1st line	36	4.5	12.3	Tutt A, SABCS 2014
Cisplatin/ Carboplatin	II	86	1st line (80.2%)	26	2.9	11.0	Isakoff SJ, J Clin Oncol, 2015
≥1st-line treatment							
Ixabepilone	II (pooled analysis)	60	Resist to AC-T or just to T	6-17	1.6-2.7	--	Perez EA, Breast Cancer Res Treat 2010
Capecitabine	III (pooled analysis)	208	Prior A, T or resist to A, T	15	1.7	--	Perez EA, Breast Cancer Res Treat 2010
Eribulin	III (pooled analysis)	199	≥1 prior chemo	11	2.8	12.4	Pivot X, Ann Oncol 2016

ORR = overall response rate; PFS = progression-free survival.

Optimizing Current Standards of Care: Key Takeaways

- Neoadjuvant chemotherapy for all except cT1,cN0
- Generally ddAC/T
- Consider adding carboplatin for higher stage, *BRCA*-mutated slow responders
- Adjuvant capecitabine for residual disease (recommend RCB classification by pathologist and using cap in RCB-2, 3)
- Neoadjuvant/adjuvant trials for PARP inhibitors in germline *BRCA*-mutated disease in progress

dd = dose dense

Recently Approved and/or Emerging Therapies in TNBC

CHEMOTHERAPY REGIMENS FOR RECURRENT OR STAGE IV (M1) DISEASE[a,b]

HER2-Negative

Preferred regimens

- Anthracyclines
  - Doxorubicin
  - Liposomal doxorubicin
- Taxanes
  - Paclitaxel
- Anti-metabolites
  - Capecitabine
  - Gemcitabine
- Microtubule inhibitors
  - Vinorelbine
  - Eribulin
- PARP inhibitors (options for patients with HER2-negative tumors and germline *BRCA1/2* mutation)[d]
  - Olaparib[d] (category 1)
  - Talazoparib[d] (category 1)
- Platinum (option for patients with triple-negative tumors and germline *BRCA1/2* mutation)[d]
  - Carboplatin
  - Cisplatin
- Atezolizumab + albumin-bound paclitaxel (option for patients with PD-L1-positive TNBC)[e]

Other recommended regimens[c]

- Cyclophosphamide
- Docetaxel
- Albumin-bound paclitaxel
- Epirubicin
- Ixabepilone

Useful in certain circumstances[c]

- AC (doxorubicin/cyclophosphamide)
- EC (epirubicin/cyclophosphamide)
- CMF (cyclophosphamide/methotrexate/fluorouracil)
- Docetaxel/capecitabine
- GT (gemcitabine/paclitaxel)
- Gemcitabine/carboplatin
- Paclitaxel/bevacizumab[f]

HER2-Positive[g]

Preferred regimens

- Pertuzumab + trastuzumab + docetaxel (category 1)[h]
- Pertuzumab + trastuzumab + paclitaxel[g]

Other recommended regimens:

- Ado-trastuzumab emtansine (T-DM1)
- Trastuzumab + paclitaxel[h] ± carboplatin
- Trastuzumab + docetaxel[h]
- Trastuzumab + vinorelbine[h]
- Trastuzumab + capecitabine
- Lapatinib + capecitabine
- Trastuzumab + lapatinib (without cytotoxic therapy)
- Trastuzumab + other agents[h,i,j]

[a] Albumin-bound paclitaxel may be substituted for paclitaxel or docetaxel due to medical necessity (ie, hypersensitivity reaction). If substituted for weekly paclitaxel or docetaxel, then the weekly dose of nab-paclitaxel should not exceed 125 mg/m².

[b] Consider scalp cooling to reduce incidence of chemotherapy-induced alopecia for patients receiving chemotherapy. Results may be less effective with anthracycline-containing regimens.

[c] Sequential single agents are preferred, but chemotherapy combinations may be used in select patients with high tumor burden, rapidly progressing disease, and visceral crisis.

[d] Patients with HER2-negative disease, strongly consider for germline *BRCA1/2* testing.

[e] Patients with TNBC, assess PD-L1 biomaker status on tumor-infiltrating immune cells to identify patients most likely to benefit from atezolizumab plus albumin-bound paclitaxel.

[f] Randomized clinical trials in metastatic breast cancer document that the addition of bevacizumab to some first- or second-line chemotherapy agents modestly improves time to progression and response rates but does not improve overall survival. The time-to-progression impact may vary among cytotoxic agents and appears greatest with bevacizumab in combination with weekly paclitaxel.

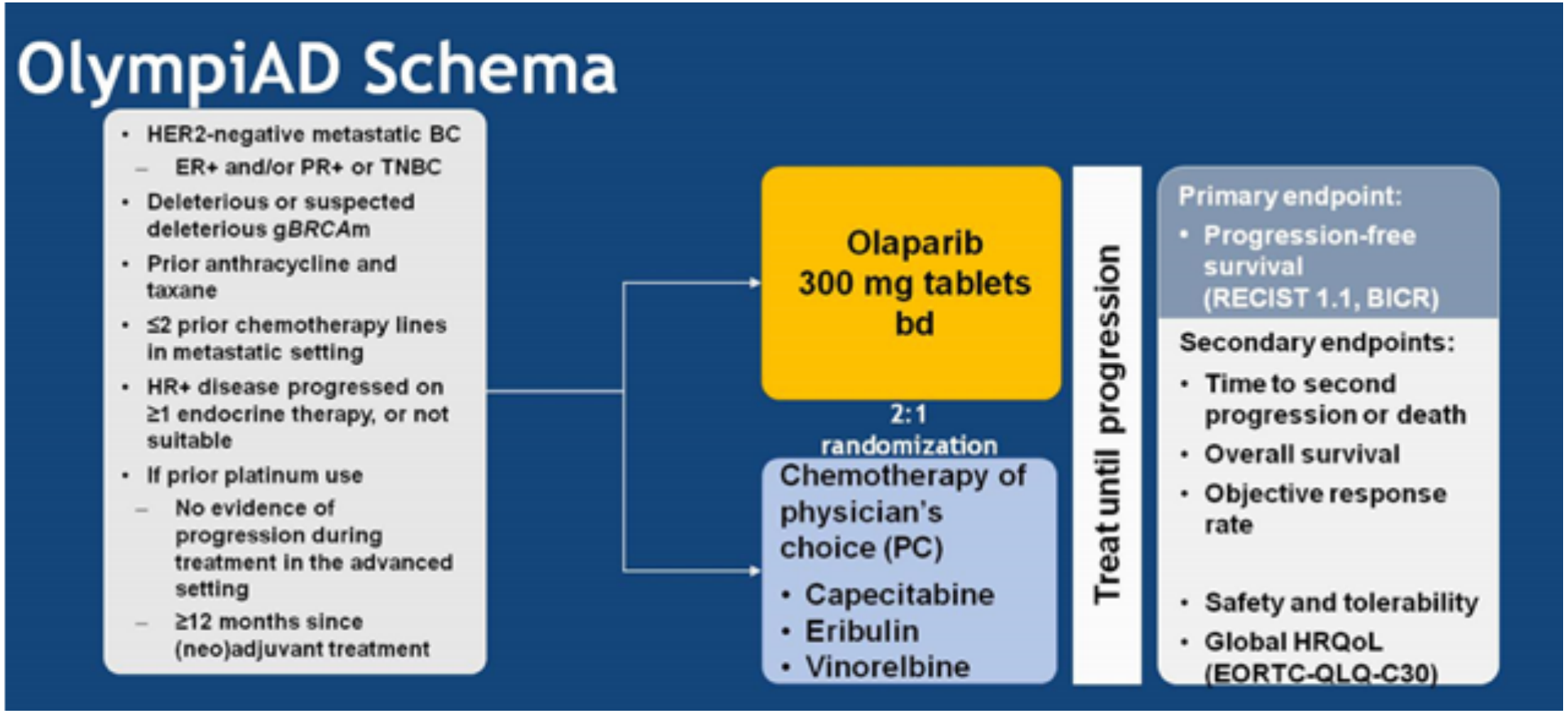
[g] Trastuzumab and hyaluronidase-oysk injection for subcutaneous use may be substituted for trastuzumab. It has different dosage and administration instructions compared to intravenous trastuzumab. Do not substitute trastuzumab and hyaluronidase-oysk for or with ado-trastuzumab emtansine.

[h] Patients previously treated with chemotherapy plus trastuzumab in the absence of pertuzumab in the metastatic setting may be considered for one line of therapy including both trastuzumab plus pertuzumab in combination with or without cytotoxic therapy (such as vinorelbine or taxane). Further research is needed to determine the ideal sequencing strategy for anti-HER2 therapy.

[i] Trastuzumab given in combination with an anthracycline is associated with significant cardiac toxicity. Concurrent use of trastuzumab and pertuzumab with an anthracycline should be avoided.

[j] Trastuzumab may be safely combined with all non-anthracycline containing preferred and other single agents listed above for recurrent or metastatic breast cancer.

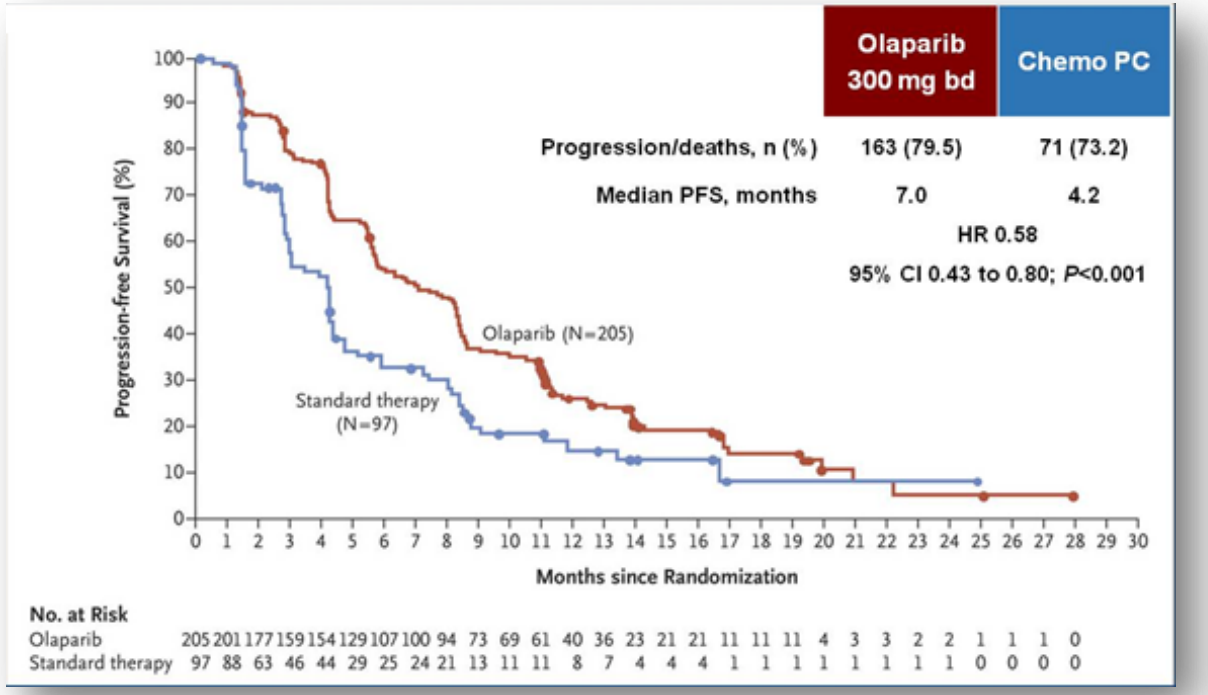
PARP Inhibitors



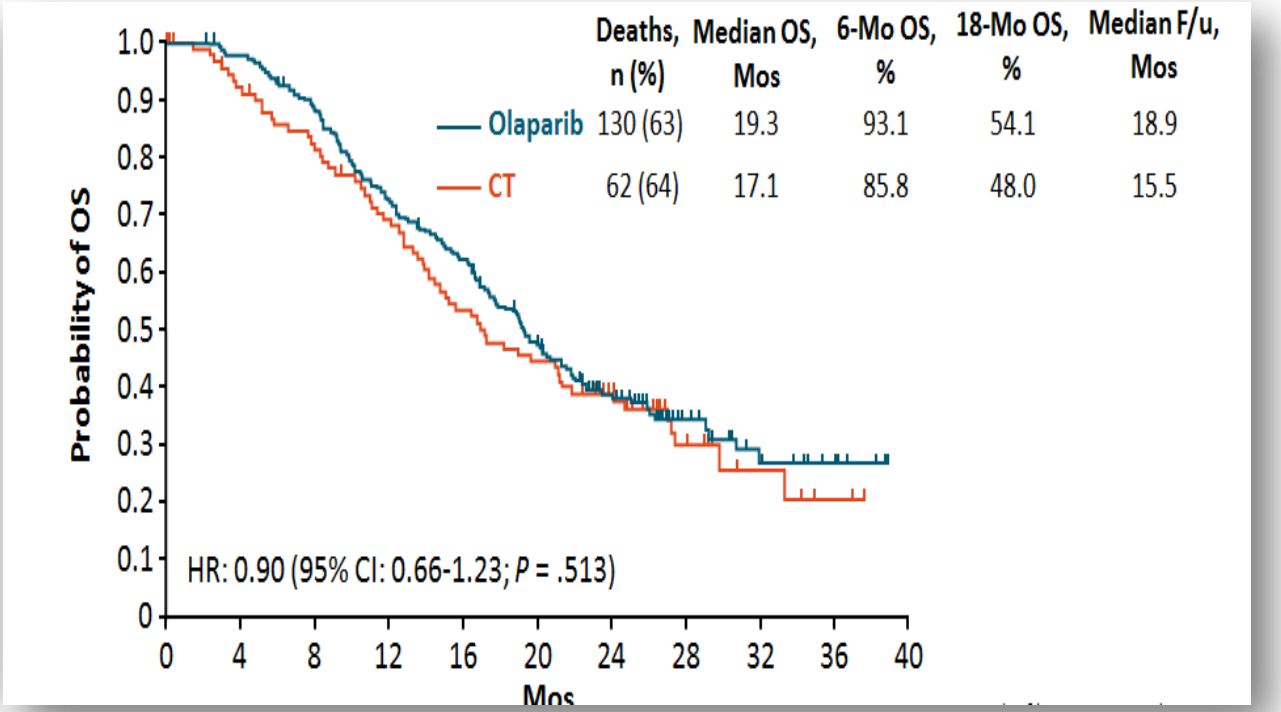
BC = breast cancer; bd = twice per day; BICR = blinded independent central review; EORTC-QLQ-C30 = European Organisation for Research and Treatment of Cancer Core Quality of Life Questionnaire; g*BRCA*m = germline *BRCA* mutation; HRQoL = health-related quality of life; RECIST = Response Evaluation Criteria in Solid Tumors

Robson M, et al. *N Engl J Med.* 2017;377:523-533.

OlympiAD Outcomes



PFS



OS

PC = physician's choice; F/u = follow-up

Robson M, et al. *N Engl J Med.* 2017;377:523-533; Robson ME, et al. *Ann Oncol.* 2019;30:558-566.

EMBRACA: Talazoparib vs. Chemotherapy in Advanced *BRCA1/2*+, HER2- Breast Cancer

- Randomized, open-label phase 3 study conducted at 145 sites in 16 countries

Stratified by HR status (ER+ and/or PgR+ vs. TNBC), prior chemo regimens (0 vs. ≥ 1), history of CNS metastases (yes vs. no)

21-day cycles

Patients with HER2-negative LA/MBC with deleterious or suspected deleterious germline *BRCA1/2* mutation; previous anthracycline and/or taxane, ≤ 3 previous lines of CT* for advanced disease (N = 431)

Talazoparib 1.0 mg PO QD (n = 287)

Physician's Choice of Chemotherapy† (n = 144)

Until PD or unacceptable AEs

- Primary endpoint: PFS by BICR
- Secondary endpoints: ORR, OS, safety
- Investigational endpoints: DoR, QoL

*Previous platinum-based therapy for EBC permitted if DFI ≥ 6 months

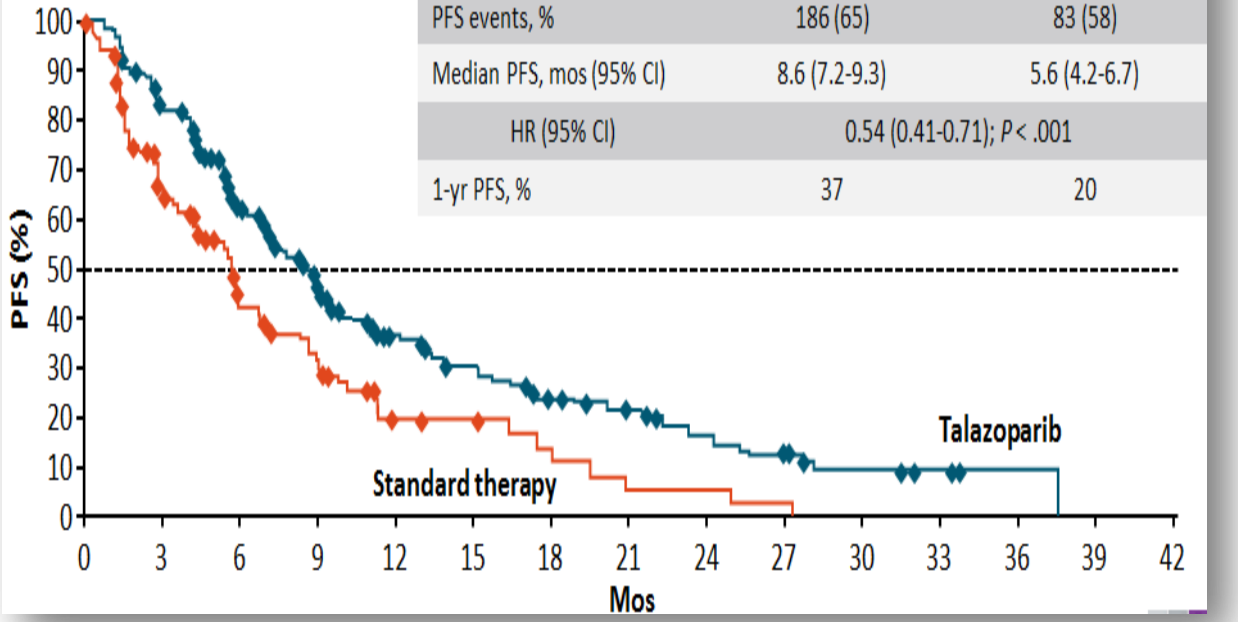
†Physician's choice of: capecitabine 1250 mg/m^2 PO BID days 1-14; eribulin 1.4 mg/m^2 IV days 1, 8; gemcitabine 1250 mg/m^2 IV days 1, 8; or vinorelbine 30 mg/m^2 IV days 1, 8, and 15

BID = twice per day; CT = chemotherapy; DFI = ; disease-free interval; DoR = duration of response; EBC = early-stage breast cancer; IV = intravenous; LA = locally advanced; MBC = metastatic breast cancer; PgR = progesterone receptor; PO = orally; QD = every day; QoL = quality of life

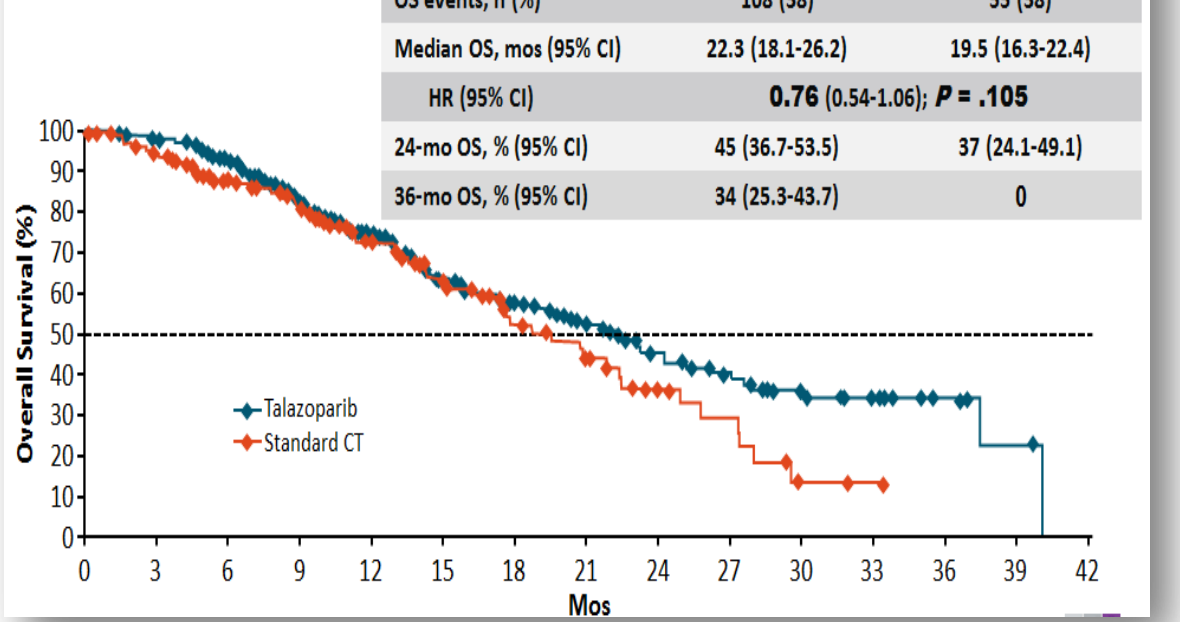
Litton JK, et al. *N Engl J Med* 2018;379:753-63.

EMBRACA: Endpoints

PFS Outcome	Talazoparib (n = 287)	Standard CT (n = 144)
PFS events, %	186 (65)	83 (58)
Median PFS, mos (95% CI)	8.6 (7.2-9.3)	5.6 (4.2-6.7)
HR (95% CI)	0.54 (0.41-0.71); *P* < .001	
1-yr PFS, %	37	20



OS Outcome	Talazoparib (n = 287)	Standard CT (n = 144)
OS events, n (%)	108 (38)	55 (38)
Median OS, mos (95% CI)	22.3 (18.1-26.2)	19.5 (16.3-22.4)
HR (95% CI)	**0.76** (0.54-1.06); ***P* = .105**	
24-mo OS, % (95% CI)	45 (36.7-53.5)	37 (24.1-49.1)
36-mo OS, % (95% CI)	34 (25.3-43.7)	0



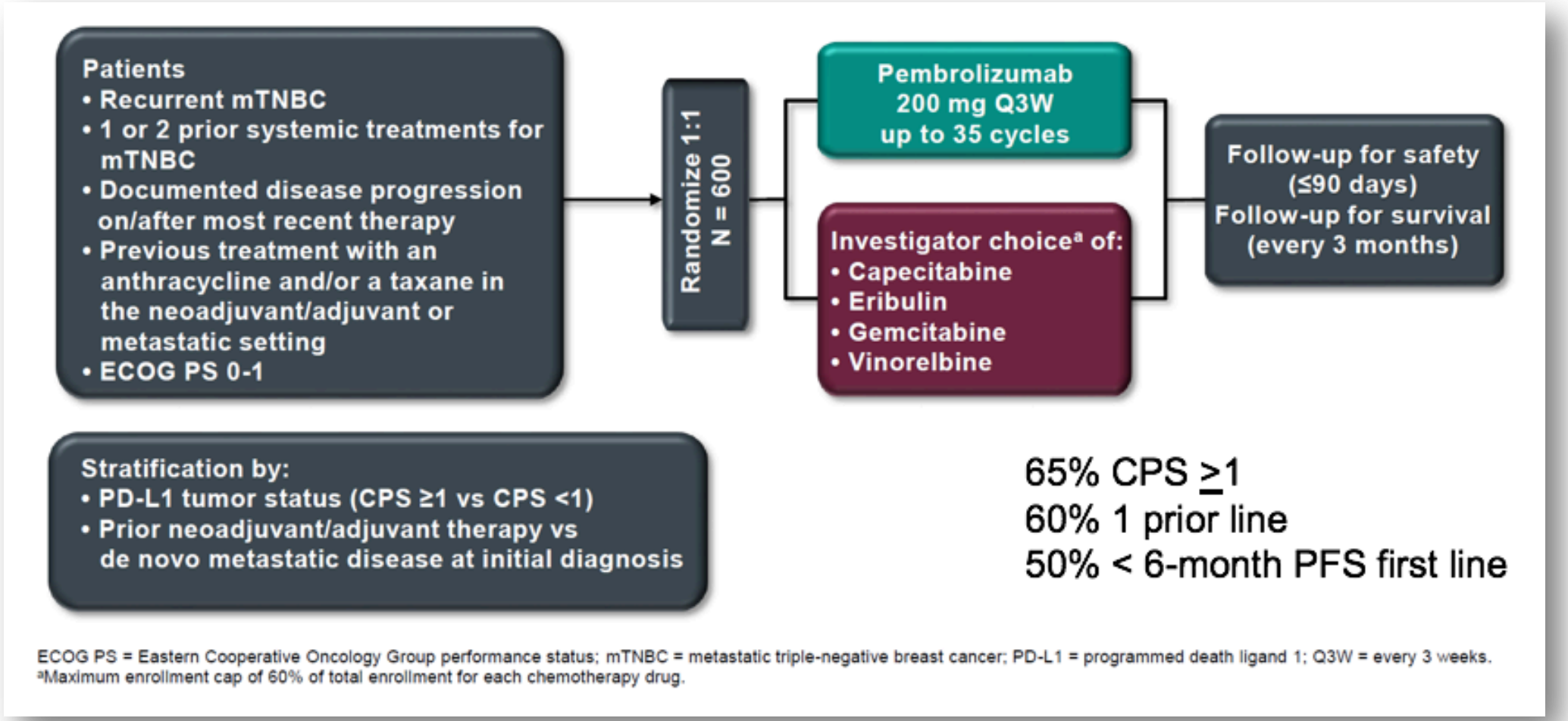
Litton JK, et al. *N Engl J Med.* 2018;379:753-63.

PD-(L)1 Inhibitors in TNBC: Monotherapy

	n	Median # prior lines therapy (range)	Agent(s)	ORR (95% CI)	Median duration response
KEYNOTE-012 (NCT01848834)	32	2 (0-9)	Pembro	18.5%	NR
KEYNOTE-086 (NCT02447003)	A (>1 prior therapy)= 170	NR	Pembro	5%	6.3 mths
	B (1st line, PD-L1+)= 52	0		23%	8.4 mths
Javelin	58	2 (1-6)	Avelu	5.2%	5.9 mths
Phase I	54 (evaluable=21)	NR	Atezo	19%	NR

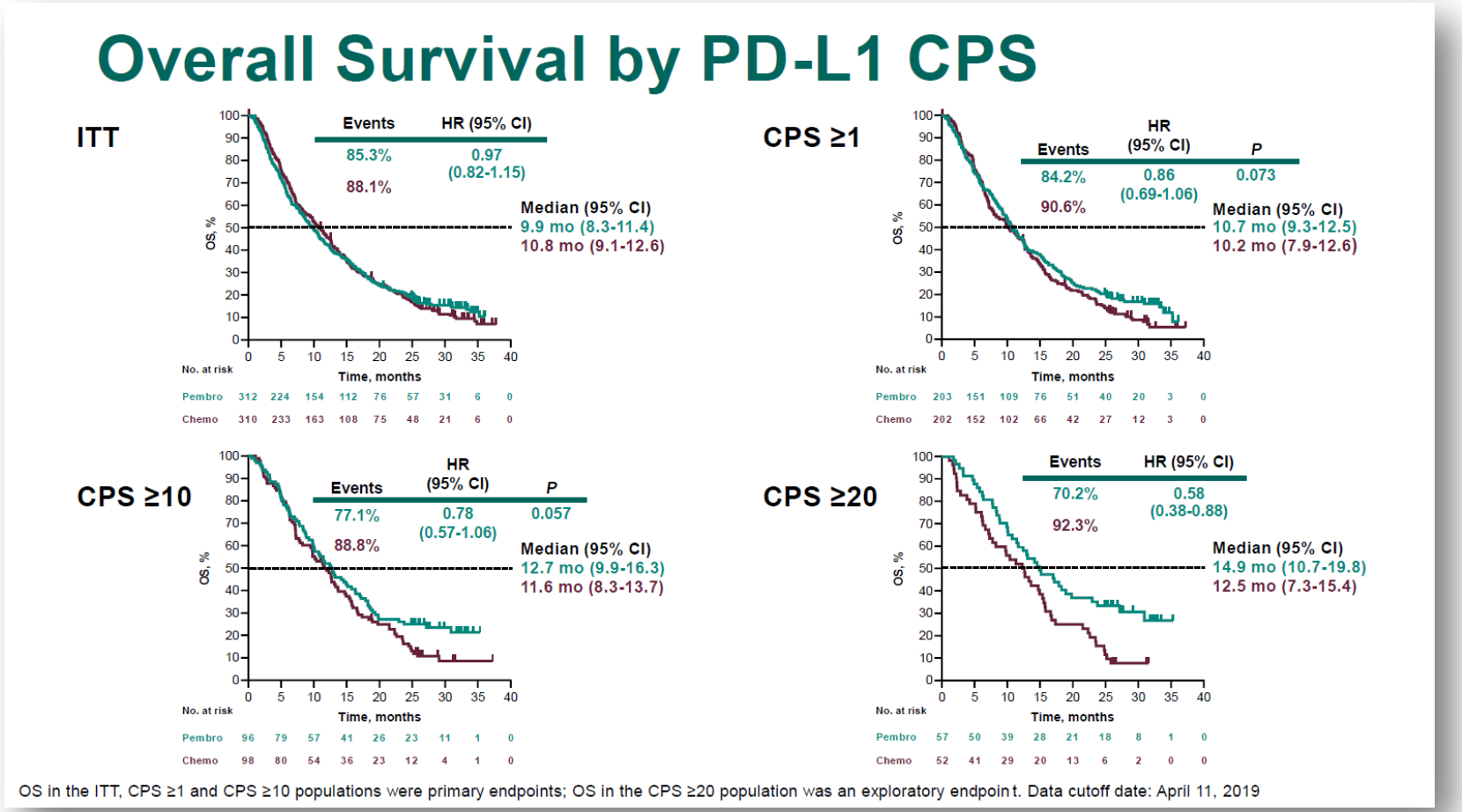
Nanda R, et al. *J Clin Oncol.* 2016;34:2460-2467; Adams S, et al. *Ann Oncol.* 2019;30:405-411; Adams S, et al. *Ann Oncol.* 2019;30:397-404; Dirix LY, et al. *Breast Cancer Res Treat.* 2018;167:671-686; Emens LA, et al. 2015 AACR Annual Meeting, Abstract 2859.

KEYNOTE-119 Study Design



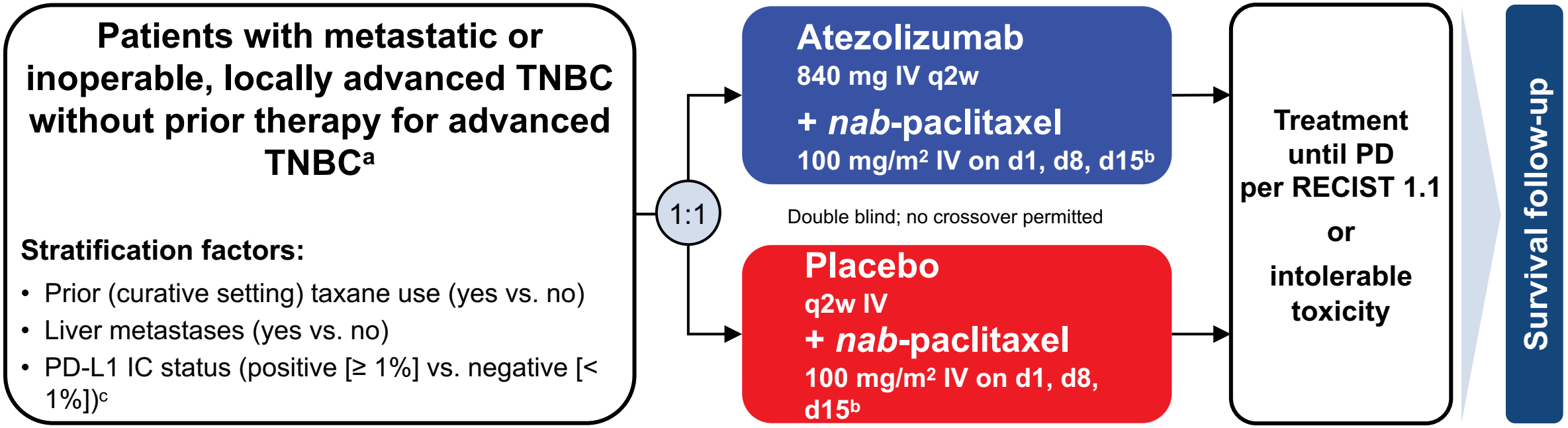
Cortes J, et al. ESMO 2019. Abstract LBA21.

KEYNOTE-119 Primary Endpoint



Cortes J, et al. ESMO 2019. Abstract LBA21.

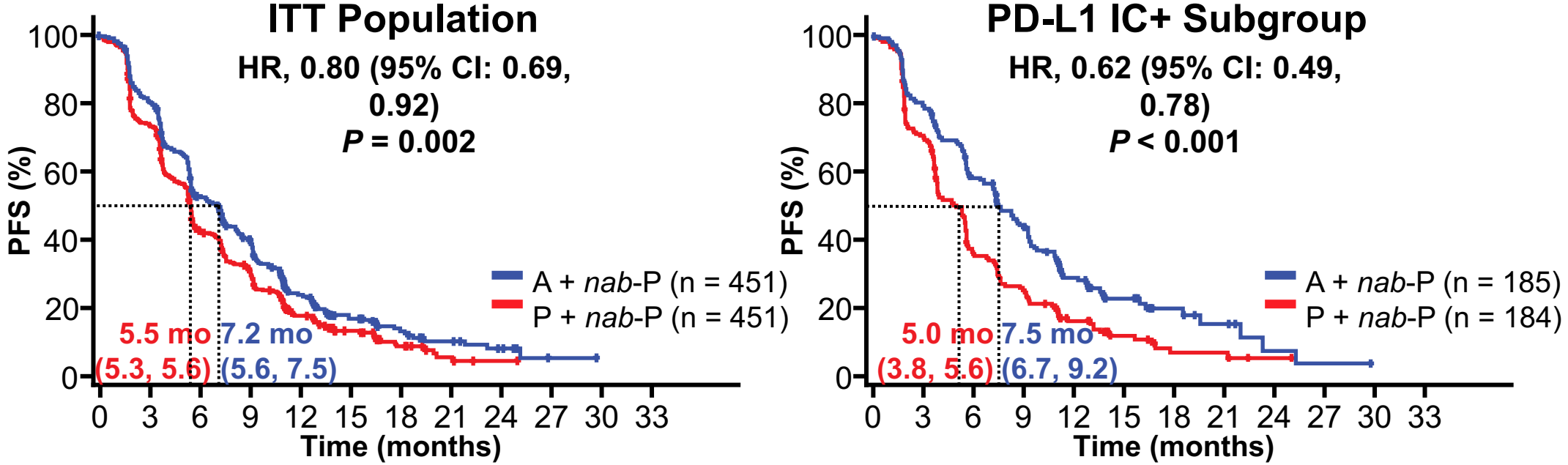
IMpassion130 Study Design



- Co-primary endpoints in ITT and PD-L1 IC+: PFS and OS[d]
- Pre-specified hierarchical testing of OS in ITT and, if significant, in PD-L1 IC+ patients
- In both treatment arms, 41% of patients were PD-L1 IC+

IC = immune cell; IHC = immunohistochemistry; PD = progressive disease; q2w = every 2 weeks
[a] Prior chemotherapy in the curative setting allowed if treatment-free interval ≥ 12 months. [b] 28-day cycle. [c] Centrally evaluated per VENTANA SP142 IHC assay.
[d] Efficacy endpoints assessed by investigators per RECIST 1.1. NCT02425891.
Schmid P, et al. *J Clin Oncol.* 2019;37 (suppl; abstr 1003).

Primary PFS Analysis in the ITT and PD-L1 IC+ Subgroup

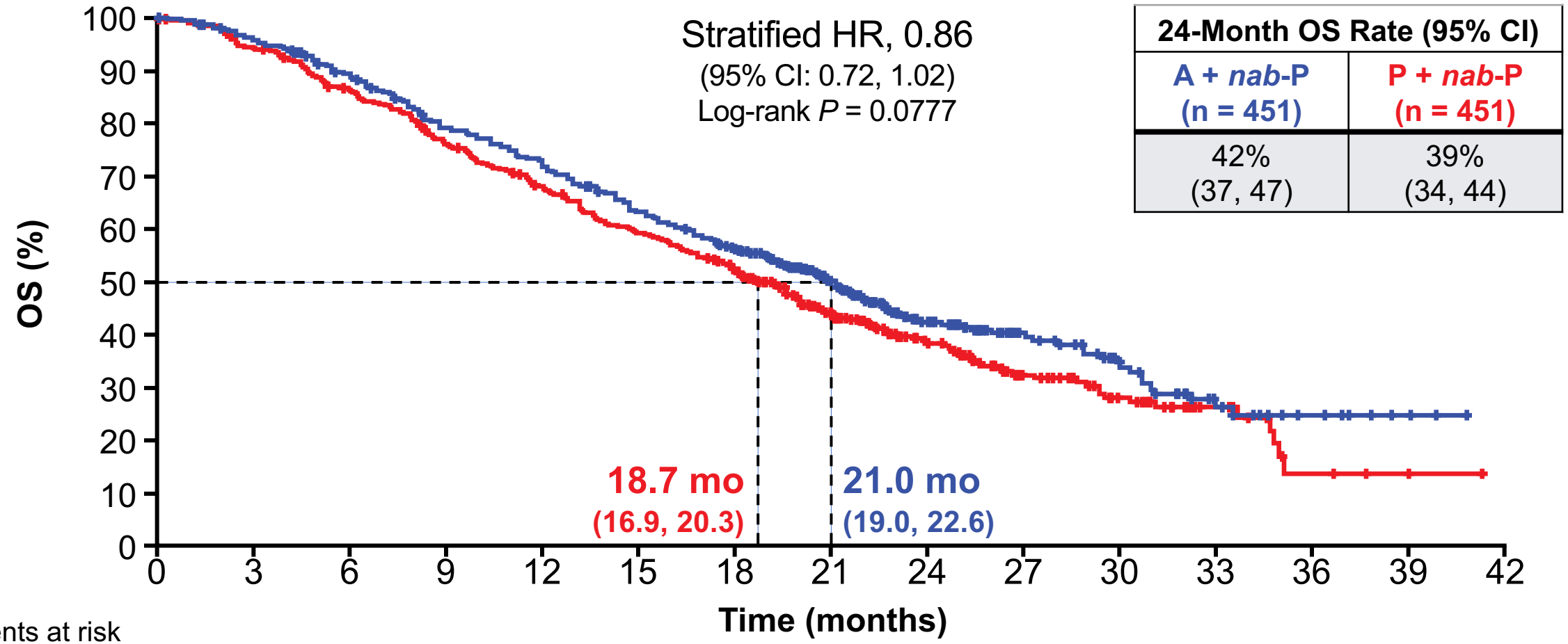


- PFS benefit driven by PD-L1 IC+ patients, as a treatment effect was not observed in PD-L1 IC− patients[1]
- Based on these data,[2] atezolizumab + nab-paclitaxel received accelerated approval by the FDA3 and is recommended for patients with PD-L1 IC+ mTNBC in the NCCN[4] and AGO[5] guidelines

AGO = Arbeitsgemeinschaft Gynäkologische Onkologie; FDA = US Food and Drug Administration; mTNBC = metastatic triple-negative breast cancer; *nab*-P = *nab*-paclitaxel; NCCN = National Comprehensive Cancer Network
Data cutoff: April 17, 2018. Median follow-up (ITT): 12.9 months.

1. Emens SABCS 2018. 2. Schmid P, et al. *N Engl J Med.* 2018;379:2108-2121; 3. Atezolizumab Prescribing Information. https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/761034s010lbl.pdf; 4. NCCN Clinical Practice Guidelines. Breast Cancer. V1.2019. 5. AGO Guidelines Breast Version 2019.1; Schmid P, et al. *J Clin Oncol.* 2019;37 (suppl; abstr 1003).

OS in ITT Population



24-Month OS Rate (95% CI)	
A + *nab*-P (n = 451)	P + *nab*-P (n = 451)
42% (37, 47)	39% (34, 44)

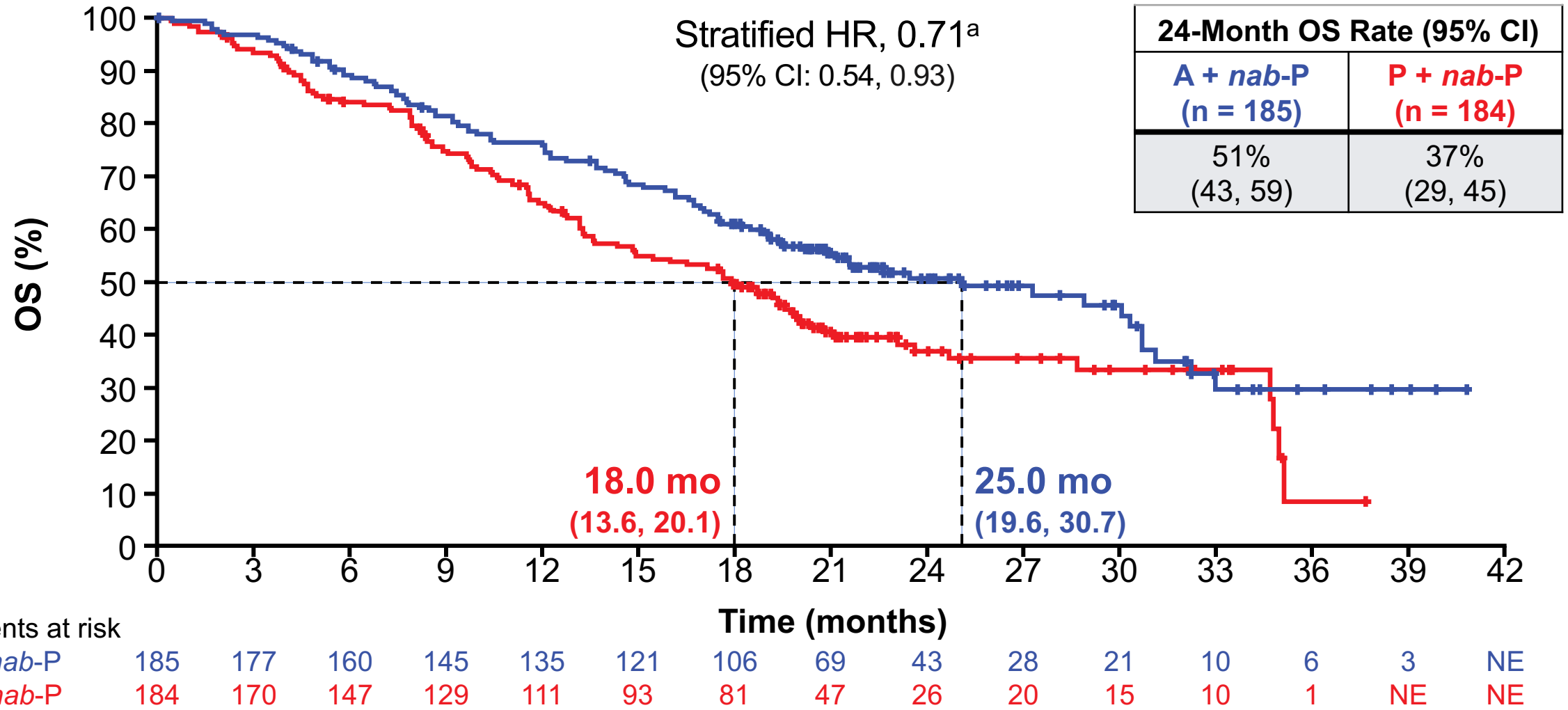
Patients at risk

A + *nab*-P	451	426	389	342	312	270	235	162	88	56	35	19	8	3	NE
P + *nab*-P	451	420	376	329	291	252	216	145	87	51	33	17	4	1	NE

NE, not estimable. Clinical cutoff date: January 2, 2019. Median PFS (95% CI) is indicated on the plot. Median follow-up (ITT): 18.0 months.

Schmid P, et al. *J Clin Oncol.* 2019;37 (suppl; abstr 1003).

OS in PD-L1+ Population



24-Month OS Rate (95% CI)	
A + *nab*-P (n = 185)	P + *nab*-P (n = 184)
51% (43, 59)	37% (29, 45)

Patients at risk

A + *nab*-P	185	177	160	145	135	121	106	69	43	28	21	10	6	3	NE
P + *nab*-P	184	170	147	129	111	93	81	47	26	20	15	10	1	NE	NE

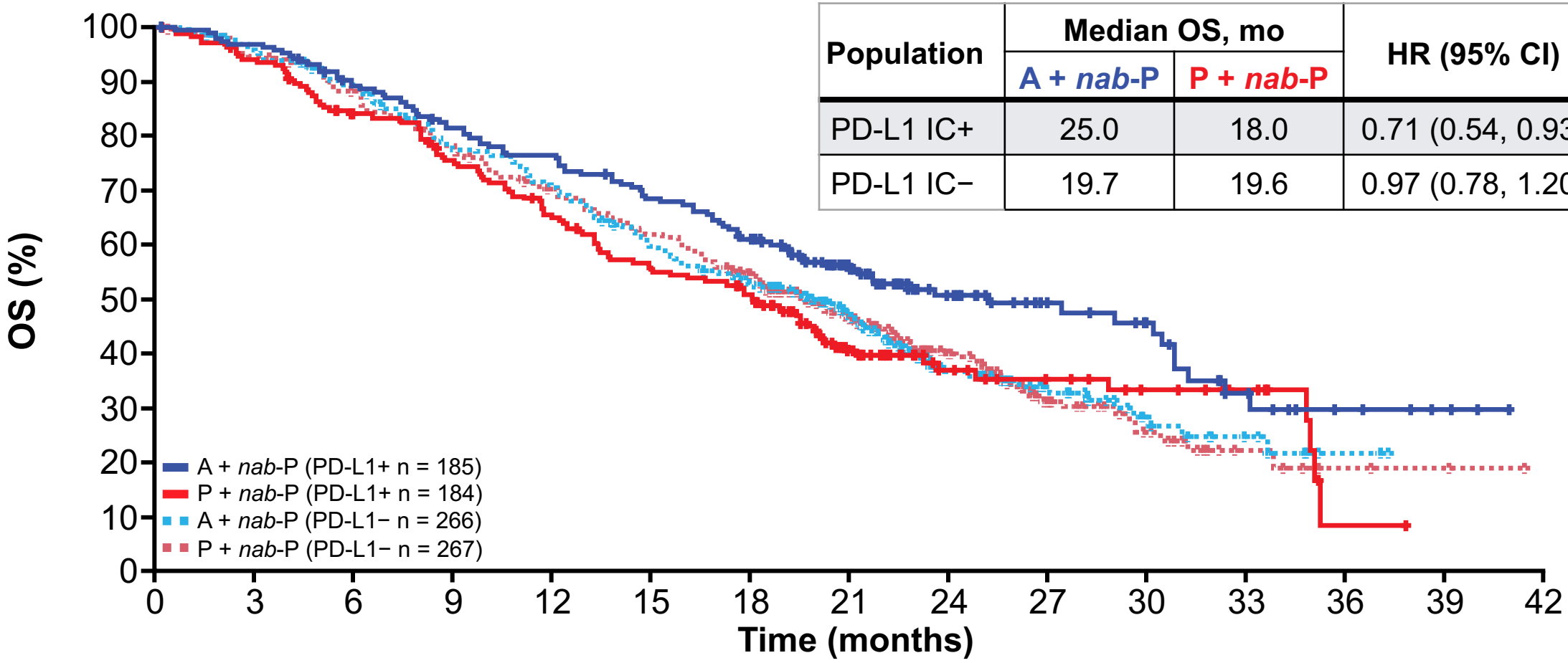
[a] Not formally tested due to pre-specified hierarchical analysis plan.

Clinical cutoff date: January 2, 2019. Median PFS (95% CI) is indicated on the plot. Median follow-up (ITT): 18.0 months.

Schmid P, et al. *J Clin Oncol.* 2019;37 (suppl; abstr 1003).

Comparison of OS in PD-L1+ and PD-L1− Populations

Population	Median OS, mo		HR (95% CI)
	A + *nab*-P	P + *nab*-P	
PD-L1 IC+	25.0	18.0	0.71 (0.54, 0.93)
PD-L1 IC−	19.7	19.6	0.97 (0.78, 1.20)



Clinical cutoff date: January 2, 2019.

Schmid P, et al. *J Clin Oncol.* 2019;37 (suppl; abstr 1003).

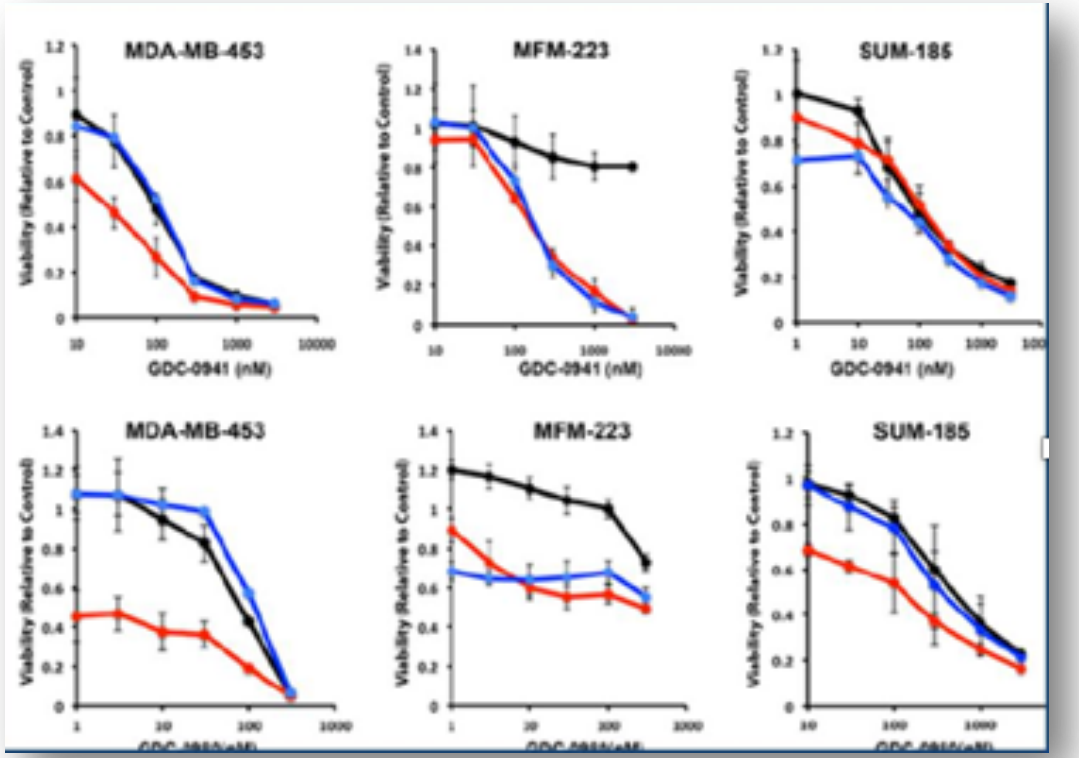
FDA Approval of Atezolizumab

- March 8, 2019: accelerated approval for atezolizumab in combination with paclitaxel protein-bound for adult patients with unresectable locally advanced or metastatic PD-L1+ TNBC
  - PD-L1–stained tumor-infiltrating IC of any intensity covering ≥ 1% of the tumor area, determined by an FDA-approved test
  - VENTANA PD-L1 (SP142) assay approved as companion diagnostic device for selecting TNBC patients for atezolizumab

FDA Website. https://www.fda.gov/drugs/drug-approvals-and-databases/fda-approves-atezolizumab-pd-l1-positive-unresectable-locally-advanced-or-metastatic-triple-negative

Androgen Receptors in TNBC: Preclinical

- Gene expression profiling (LAR subtype)
  - Molecular signature suggested an active hormonally regulated transcription program
  - Genes known to be either direct targets of ER or responsive to estrogen
- Evidence that androgen enhanced the growth of MDA-MB-453 breast cancer cells
- Adrenal steroids inhibit growth of AR+, ER- breast cancer cell lines



LAR = luminal androgen receptor

Lehmann BD, et al *J Clin Invest* 2011;121:2750-67; Garreau JR, et al. *Am J Surg* 2006;191:576-80; Doane AS, et al. *Oncogene* 2006;25:3994-4008.

Phase 2: Enzalutamide

- AR+ TNBC
  - ITT = AR > 0%, one dose enzalutamide
    - N=118
    - 78 evaluable
- Enzalutamide 160 mg/day orally

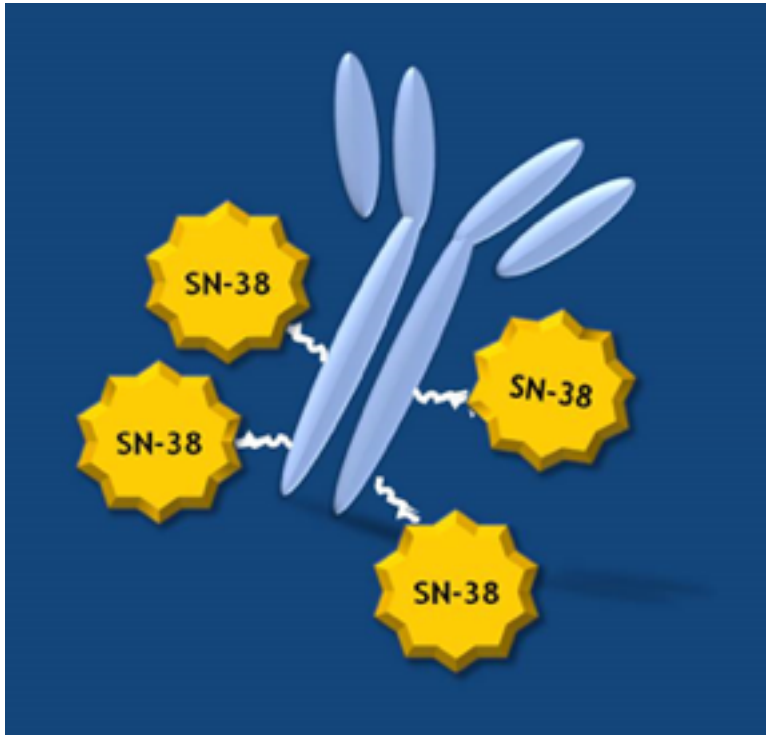
- Median PFS
  - ITT 2.9 mos (95% CI, 1.9-3.7 mos)
  - Evaluable 3.3 mos (95% CI, 1.9-4.1 mos)
- CBR (4 month)
  - ITT 25% (95% CI, 17-33)
  - Evaluable 33% (95% CI, 23-45)
- CBR (6 month)
  - ITT 20% (95% 14-29)
  - Evaluable 28% (95% 19-39)
- CR or PR
  - ITT 6%
  - Evaluable 8%

CBR = clinical benefit rate; CR = complete response; PR = partial response

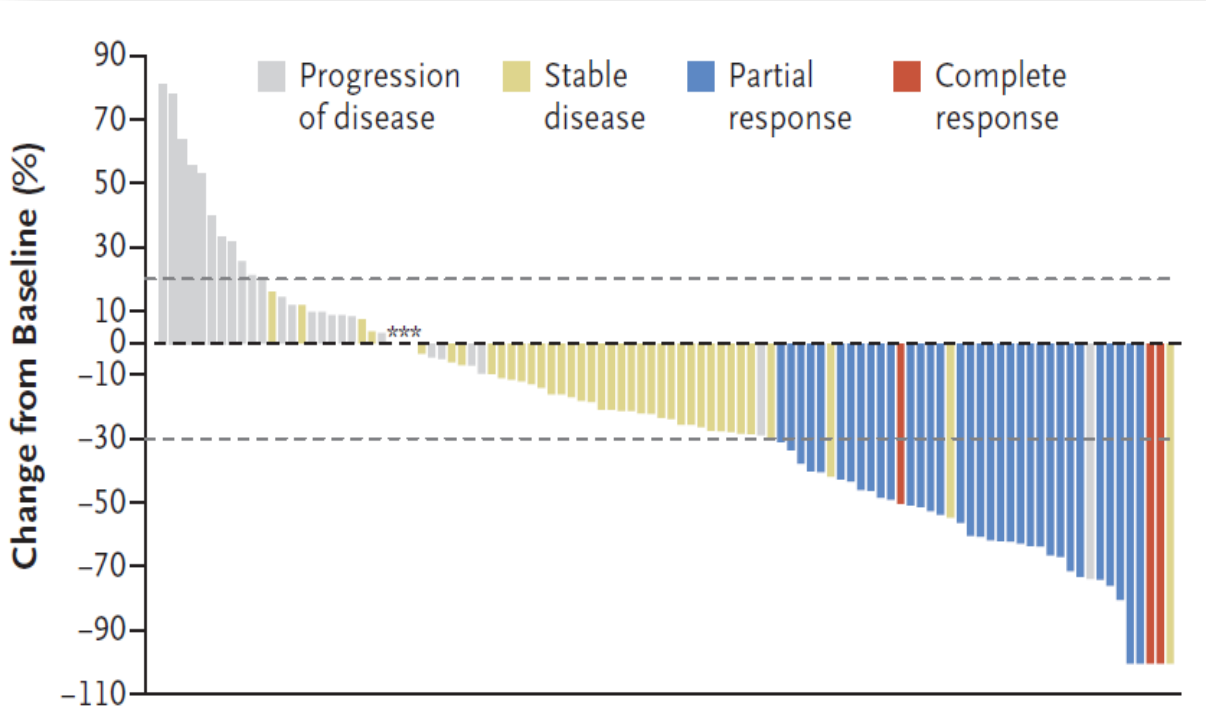
Traina TA, et al. *J Clin Oncol.* 2018;36:884-890.

Sacituzumab Govitecan

- Anti-Trop-2 antibody
  - Trop-2 expressed in up to 80% of TNBCs
- Linked to SN-38 (active metabolite of irinotecan)

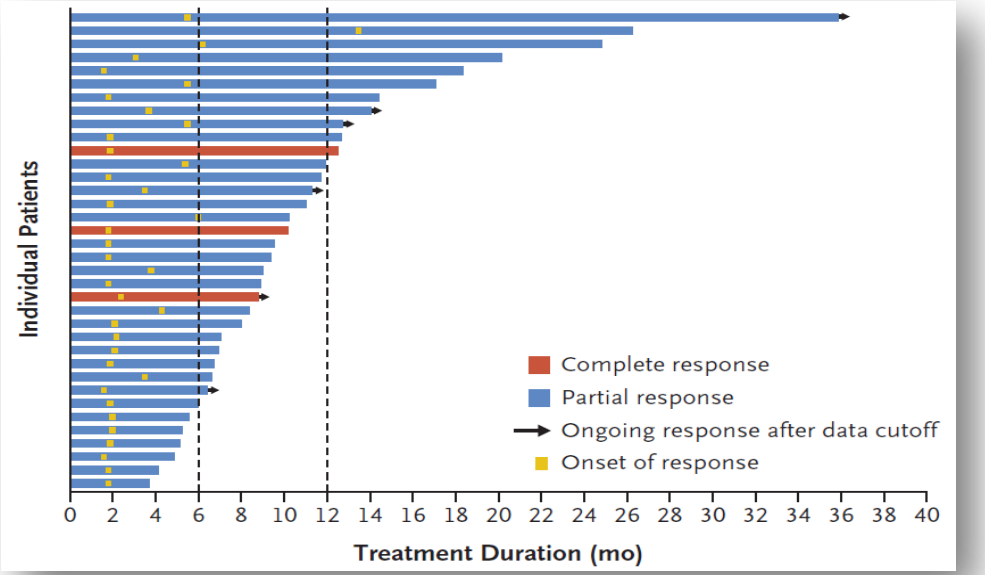


Sacituzumab Govitecan: Efficacy in Heavily Pretreated TNBC



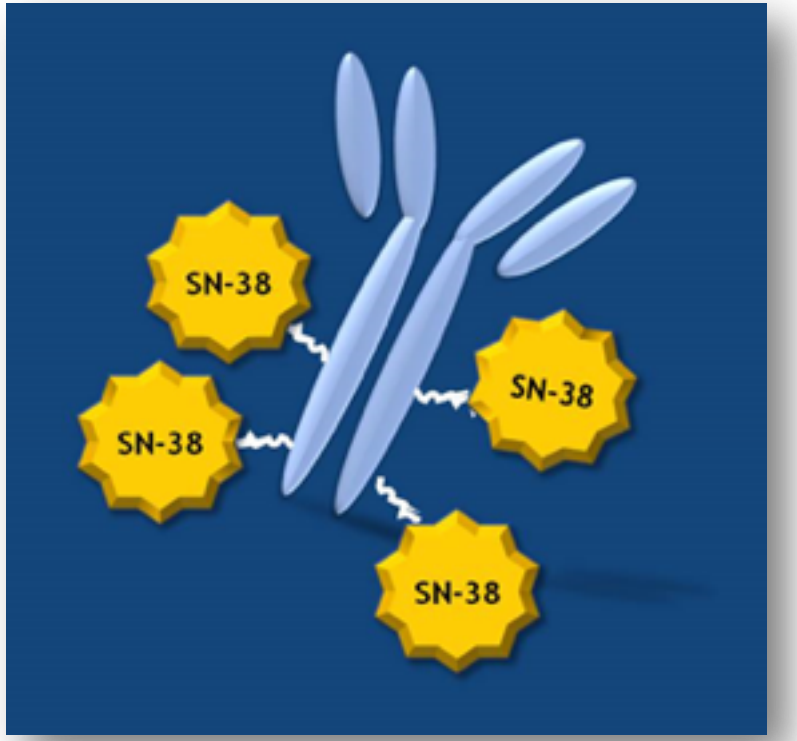
N=108
Response rate: 33.3%
CR: 2.8%
PR: 30.6%
CBR: 45.4%

Duration of response



Bardia A, et al *N Engl J Med.* 2019;380:741-751.

Sacituzumab Govitecan: Toxicity in TNBC



Adverse Event	All Grades, No. (%)	Grades ≥ 3, No. (%)
Nausea	51 (74)	5 (7)
Neutropenia	47 (68)	27 (39)
Diarrhea	41 (59)	9 (13)
Anemia	38 (55)	10 (14)
Vomiting	35 (51)	7 (10)
Fatigue	35 (51)	6 (9)
Febrile neutropenia	5 (7)	5 (7)

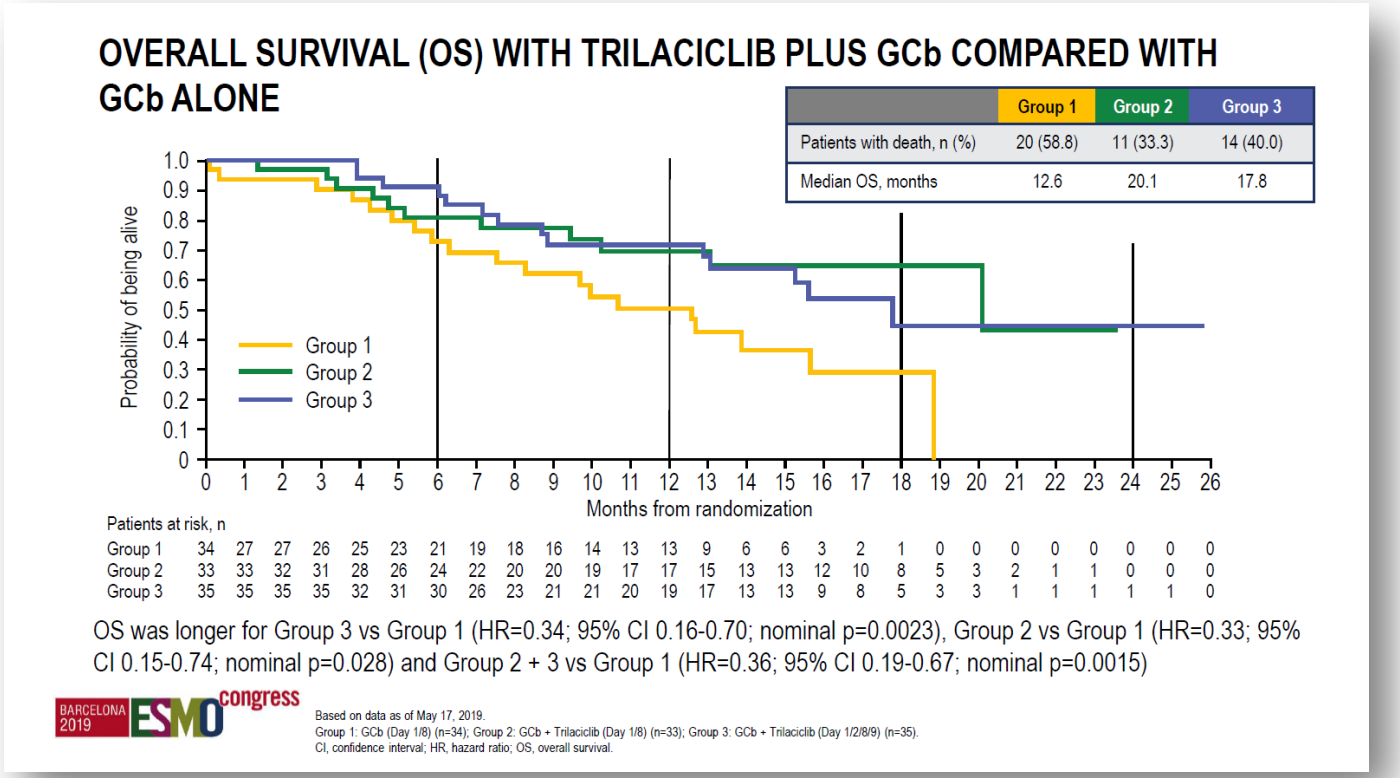
Bardia A, et al *N Engl J Med.* 2019;380:741-751.

Small Molecules in Development for TNBC

- Trilaciclib (CDK 4/6i)
- AKT inhibitors
- HDAC inhibitors

HDAC = histone deacetylase

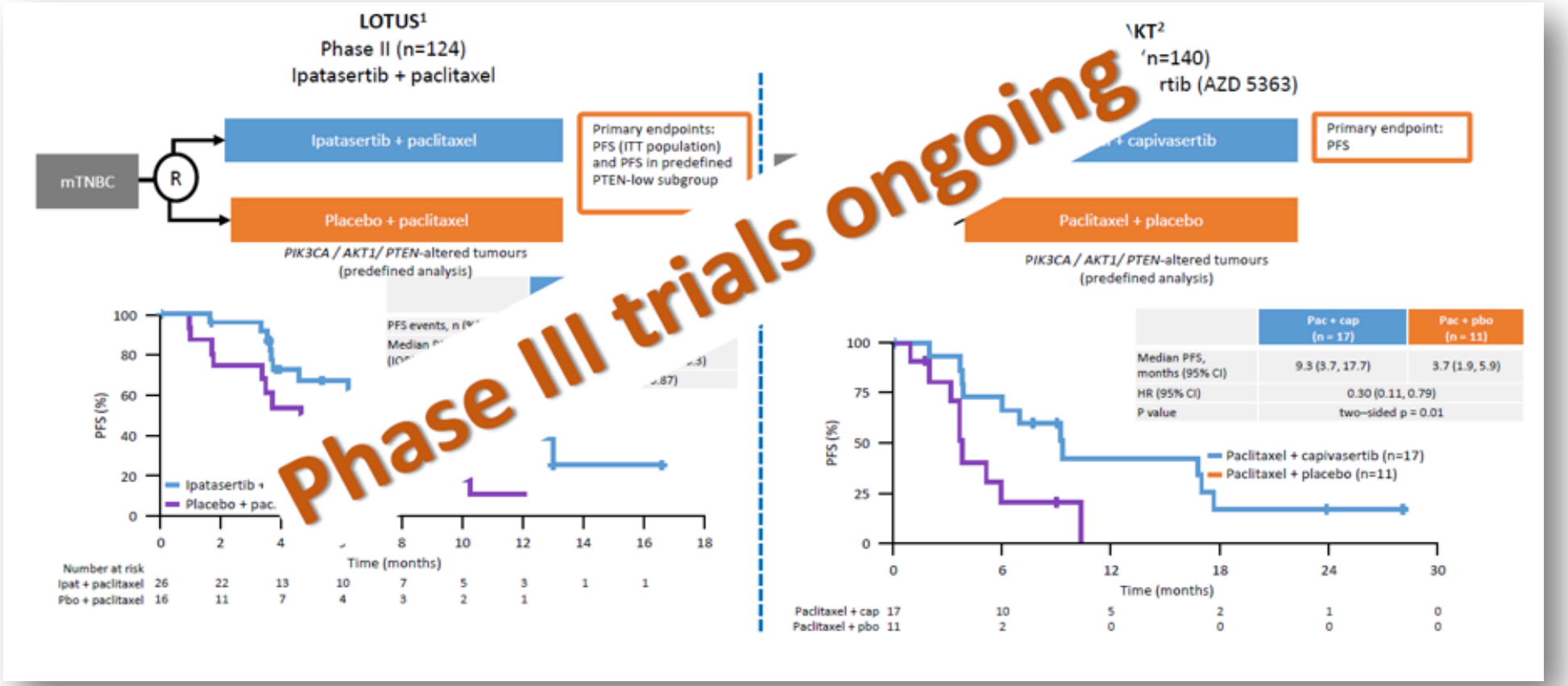
Trilaciclib: Novel CDK4/6 Inhibitor



- Tested in randomized phase 2 trial
- Primary endpoint: reduction in neutropenia
- Negative for primary endpoint, and for secondary endpoint of PFS

Tan AR, et al. *Lancet Oncol.* 2019 Sep 27. Epub ahead of print.

AKT Inhibitors and PIK3CA/AKT1/PTEN-Altered Metastatic TNBC



Kim SB, et al. *Lancet Oncol*. 2017;18:1360-1372; Dent R, et al. *J Clin Oncol.* 2018;36 (suppl; abstr 1008); Schmid P, et al. *J Clin Oncol.* 2018;36 (suppl; abstr 1007).

Newly Approved and/or Emerging Therapies in TNBC: Key Takeaways

- If PD-L1+: atezolizumab and nab-paclitaxel
- If g*BRCA*m+: PARP inhibitor
- If neither:
  - Comprehensive genomic profiling
  - Clinical trial
  - Taxane if >6-12 months since last taxane
  - Don’t forget anthracyclines
  - Otherwise eribulin or other agent
- Watch CNS
- Eagerly await sacituzumab and other agents

AEs Associated With PARP Inhibitors and Management Strategies

Olaparib

- OlympiAD trial
- 97% patients experienced some AE
  - 61% grade 1/2
  - Lower grade 3/4 than control arm (37% vs. 51%)
- Most common (>20%): anemia, neutropenia, nausea/vomiting, diarrhea, and fatigue
  - Only grade 3/4 toxicity (>10%) was anemia (16%)

Caulfield S, et al. *J Adv Pract Oncol.* 2019;10:167-174.

OlympiAD: AEs Associated With Olaparib (>20% Patients)

Event	All Grades (%)	Grades 3/4 (%)
Anemia	40	16
Neutropenia	27	9
Nausea	58	0
Vomiting	30	0
Diarrhea	21	0.5
Fatigue	29	3
Headache	20	1
Respiratory tract infections	27	1

Olaparib Prescribing Information. https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/208558s000lbl.pdf; Caulfield S, et al. *J Adv Pract Oncol.* 2019;10:167-174.

Olaparib: Dosing and Modifications

- Olaparib 300 mg BID
- 25% of patients required dose reductions due to AEs
  - Most common due to anemia (14%)
- 35% of patients required dose delays or interruptions
- Only 5% required permanent discontinuation
- Consider dose interruption/modifications

Caulfield S, et al. *J Adv Pract Oncol.* 2019;10:167-174.

Olaparib: Dose Adjustments for AEs

Cause	Recommendation
CYP34A inhibitors/inducers	100-150 mg BID
Renal impairment (CrCl 31-50 mL/min)	200 mg BID
Toxicity: First occurrence	250 mg BID or 200 mg BID
Second occurrence	200 mg BID or 100 mg BID
Hepatic impairment (Child-Pugh A-B)	No adjustment
MDS/AML or pneumonitis	Permanent D/C

AML = acute myeloid leukemia; CrCl = creatinine clearance; D/C = discontinuation; MDS = myelodysplastic syndrome

Olaparib Prescribing Information. https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/208558s000lbl.pdf; Caulfield S, et al. *J Adv Pract Oncol.* 2019;10:167-174.

Olaparib: Warnings

- MDS/AML (<1.5%)
  - All had received previous chemotherapy with platinum or alkylating agents
  - For prolonged heme toxicities, not recovered to grade ≤1 after 4 weeks, consider additional workup including bone marrow biopsy
- Pneumonitis (<1%)
- Potentially teratogenic
  - Contraception during and ≥ 6 months after completion of therapy

Olaparib Prescribing Information. https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/208558s000lbl.pdf; Caulfield S, et al. *J Adv Pract Oncol.* 2019;10:167-174.

Olaparib: Patient Education

- Two 150-mg tabs 12 hours apart, with or without food
- Cannot be crushed, chewed, or dissolved
- Avoid grapefruit/juice, Seville oranges/juice
- Call physician's office if patient develops:
  - Severe weakness
  - Fever
  - Signs/symptoms infection
  - Blood in urine/stool
  - Uncommon bruising or bleeding that doesn't stop
  - Shortness of breath
  - Cough
  - Nausea/vomiting or diarrhea

Talazoparib

- EMBRACA trial
- 65% of patients required dose interruptions for any-grade AE
- 53% of patients required dose reductions
- 5% patients required permanent D/C
  - Anemia (0.7%)
  - Neutropenia (0.3%)
  - Thrombocytopenia (0.3%)
- Most common AEs (>20%): fatigue, anemia, nausea/vomiting, neutropenia, headache, thrombocytopenia, alopecia, diarrhea, decreased appetite

Talazoparib Prescribing Information. https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/211651s000lbl.pdf.

EMBRACA: AEs Associated With Talazoparib (>20% Patients)

AE	Grade 1-4 (%)	Grade 3/4 (%)
Anemia	53	39
Neutropenia	35	21
Thrombocytopenia	27	15
Decreased appetite	21	<1
Headache	33	2
Nausea	49	<1
Vomiting	25	2
Diarrhea	22	1
Alopecia	25	0

Talazoparib Prescribing Information. https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/211651s000lbl.pdf.

Talazoparib: Dosing and Modifications

Recommended Starting Dose	1-mg Capsule QD
First dose reduction	0.75 mg (three 0.25-mg caps) QD
Second dose reduction	0.5 mg (two 0.25-mg caps) QD
Third dose reduction	0.25 mg QD
Fourth dose reduction	Permanent D/C

- Consider interruption with or without dose reduction, based on severity and clinical presentation (individualization)
- Recommended starting dose for patients with moderate renal impairment (CrCl 30-59 mL/min) = 0.75 mg QD
- Dose reduction with co-administration of P-gp inhibitors (amiodarone, carvedilol, clarithromycin, itraconazole, verapamil)

Talazoparib Prescribing Information. https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/211651s000lbl.pdf.

Talazoparib: Dose Modifications

Toxicity	Hold	Resume
Hgb <8 g/dL	≥9 g/dL	With dose reduction
Platelets <50,000/uL	≥75,000/uL	With dose reduction
ANC <1,000/uL	≥1,500/uL	With dose reduction
Non-heme grade 3/4	≤ grade 1	Consider dose reduction or D/C

ANC = absolute neutrophil count; Hgb = hemoglobin

Talazoparib Prescribing Information. https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/211651s000lbl.pdf.

Talazoparib: Warnings

- MDS/AML (0.3%)
  - Two patients at 4 and 24 months, respectively
  - Both received prior chemotherapy with platinum/alkylating agents
- Myelosuppression grade ≥3; anemia (39%), neutropenia (21%), and thrombocytopenia (15%)
  - Do not start talazoparib until resolution of previous heme toxicities
- Embryo-fetal toxicity
  - Use contraception during and at least 7 months after discontinuation

Talazoparib Prescribing Information. https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/211651s000lbl.pdf.

Talazoparib: Patient Education

- One 1-mg capsule daily with or without food
- Cannot be crushed, chewed, dissolved, or opened
- Call physician's office if patient develops
  - Severe weakness
  - Fatigue
  - Fever
  - Sign/symptoms of infection
  - Unusual bleeding or bruising
  - Shortness of breath

Talazoparib Prescribing Information. https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/211651s000lbl.pdf.

Case Study 1

- 89-year-old female, ECOG PS 1-2,
- PMH: hypertension, hyperlipidemia, type 2 diabetes, coronary artery disease
- 1993: Diagnosed with node-positive breast cancer
  - S/p left-sided mastectomy, radiation therapy, CMF and tamoxifen
- April 2016: new right-sided breast cancer 1.8 cm, grade 3 IDC, ER-/PR-/HER2-; ki67 37% s/p mastectomy [pT1c pN0(sn)]
- Sister and niece g*BRCA2*m→ prompted patient to get tested
- g*BRCA2*m
- Declined adjuvant chemotherapy

CMF = cyclophosphamide, methotrexate, and 5-fluorouracil; ECOG PS = Eastern Cooperative Oncology Group Performance Status; IDC = invasive ductal carcinoma; PMH = past medical history

Case Study 1

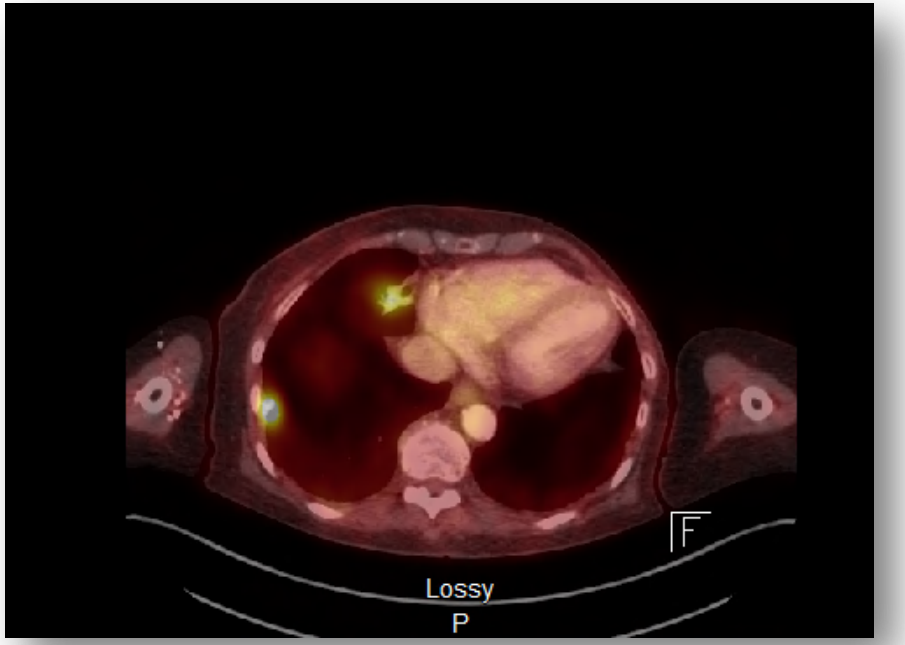
- April 2019: Develops persistent cough; outside CT showed RLL 2.8-cm nodule, right hilar/mediastinal adenopathy
- Lung bx: Metastatic poorly differentiated carcinoma, consistent with breast cancer, ER-/PR-/HER2-

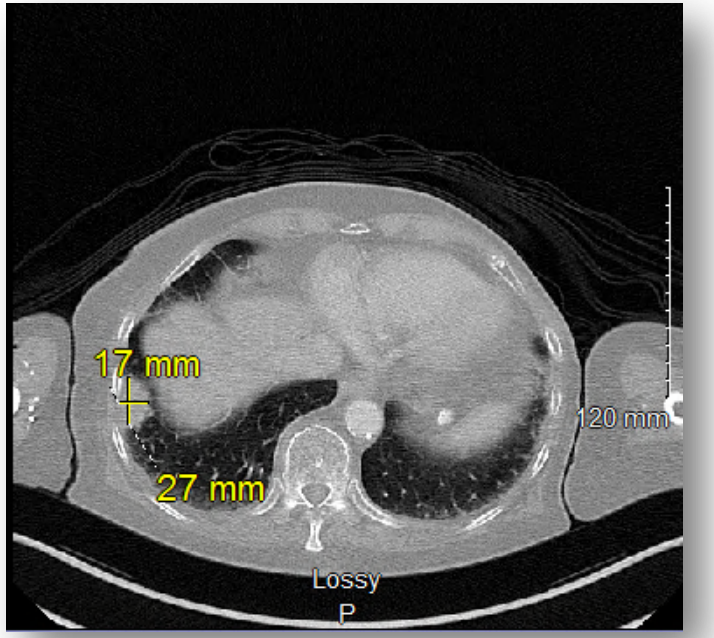
BIOMARKER	METHOD	RESULT	THERAPY ASSOCIATION		BIOMARKER LEVEL*
BRCA2	**NGS**	**Mutated, Pathogenic Exon 16 | c.7618-1G>A**	BENEFIT	**olaparib, talazoparib**	**Level 1**
			BENEFIT	carboplatin, cisplatin	Level 3A
PD-L1 (SP142)	**IHC**	**Positive, IC: 15%**	BENEFIT	**atezolizumab + nab-paclitaxel**	**Level 1**
ER	IHC	Negative | 0	LACK OF BENEFIT	endocrine therapy	Level 1
ERBB2 (Her2/Neu)	CISH	Not Amplified	LACK OF BENEFIT	ado-trastuzumab emtansine (T-DM1), lapatinib, neratinib, pertuzumab, trastuzumab	Level 1
	IHC	Negative | 0			
PR	IHC	Negative | 0	LACK OF BENEFIT	endocrine therapy	Level 1
AR	IHC	Negative | 0	LACK OF BENEFIT	bicalutamide, enzalutamide	Level 3A

CISH = chromogenic in situ hybridization; CT = computed tomography; NGS = next-generation sequencing; RLL = right lower lobe

Case Study 1

- PET/CT May 2019: mediastinal, right hilar nodal metastases and RLL metastasis





PET = positron emission tomography

Case Study 1

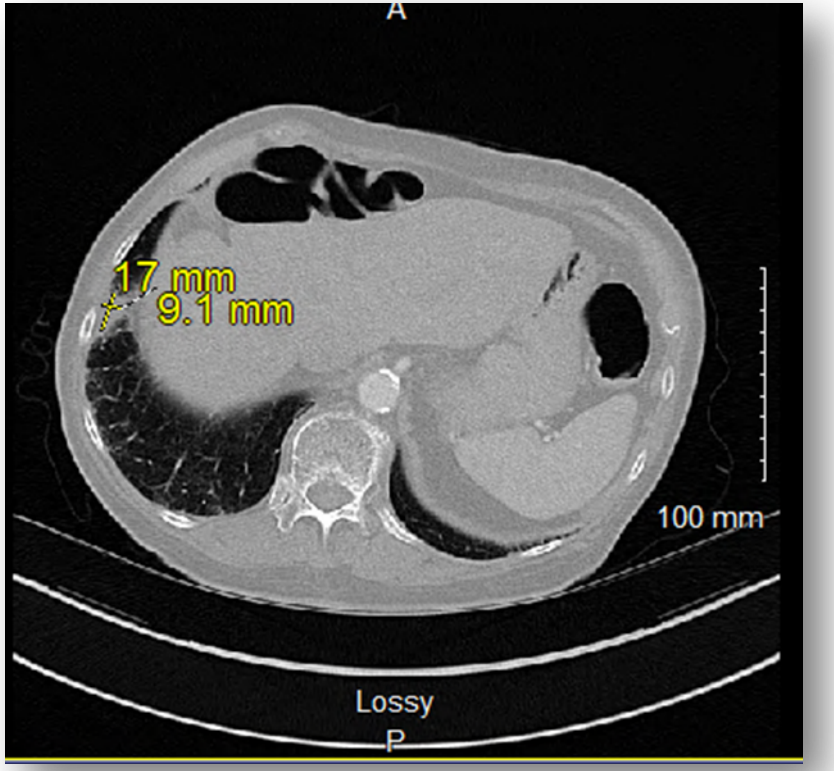
- Started olaparib 300 mg BID 5/28/19
- Fatigue, anemia 7/2/19
- Required dose interruption 7/30/19; very symptomatic, required one unit PRBC
- Restarted 8/6/19
- Dose reduced to 250 mg BID 8/20/19

Result	9/11/2019 12:50:00 PM	8/27/2019 11:23:00 AM	8/20/2019 1:20:00 PM	8/6/2019 10:47:00 AM	7/30/2019 10:44:00 AM	7/2/2019 1:13:00 PM	5/28/2019 3:48:00 PM
*** CBC ***							
WBC	3.0	4.2	4.0	6.5	5.3	5.2	8.2
ANC	1.30	2.50	2.00	3.30	2.80	2.60	4.10
HGB	8.9	8.1	8.7	10.3	7.7	9.9	12.9
HCT	27.2	23.6	26.7	32.0	23.6	28.9	37.6
MCV	93.9	92.1	93.2	92.2	88.5	90.4	92.4
Plat	317.0	155.0	162.0	238.0	282.0	224.0	213.0
MCHC	32.7	34.4	32.6	32.2	32.6	34.5	34.2

PRBC = packed red blood cells

Case Study 1

- CT 8/27/19 showed decrease in size of RLL nodule and mediastinal adenopathy
- Continues on olaparib 250 mg BID as of today!



AEs Associated With PARP Inhibitors and Management Strategies: Key Takeaways

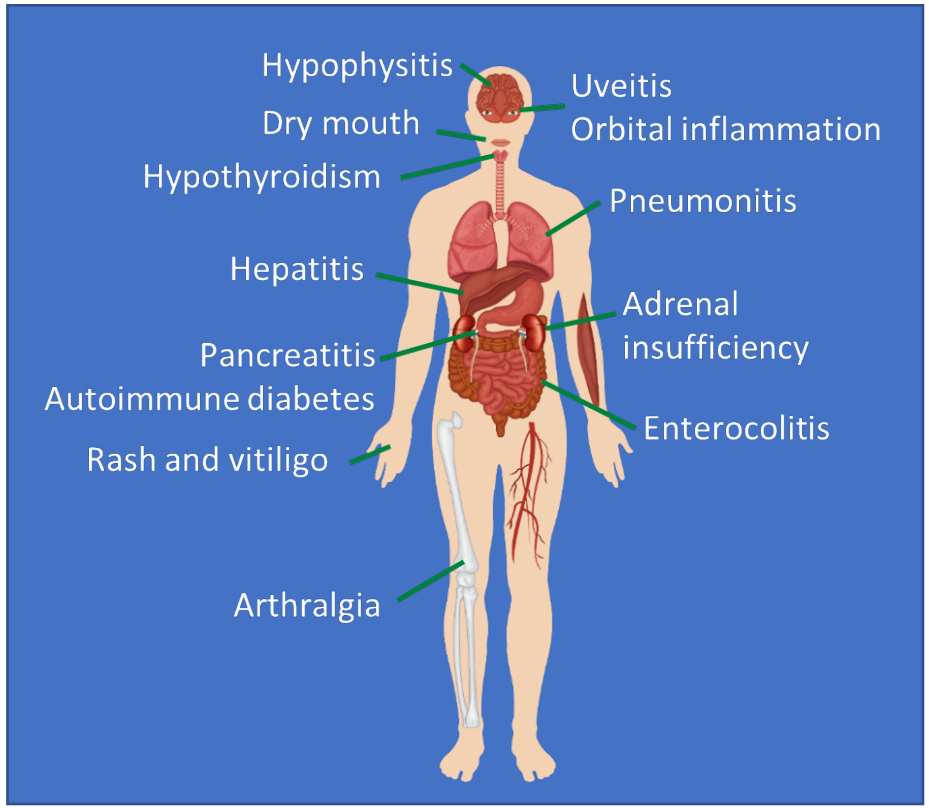
- Monitor CBC at baseline and at least monthly
- High index of suspicion for pneumonitis or AML workup depending on clinical presentation
- Ensure oral medication compliance
- Educate on use of antiemetics and antidiarrheals
- Evaluate concomitant medications routinely
- Be familiar with dose modifications, and consider if dose delay/interruption is not effective

CBC = complete blood count

irAEs Associated With ICIs and Management Strategies

Spectrum of Toxicity

- Checkpoint inhibitors stimulate the immune environment and can cause irAEs
- irAEs differ from AEs with chemotherapy and targeted therapy
- Most occur within first few weeks, but can occur any time—even after therapy
- Typically mild, but can be severe, irreversible, or life-threatening
- irAEs do not occur in all patients
- Reasons are unknown



irAEs = immune-related adverse events

Brahmer JR, et al. *J Clin Oncol.* 2018;36:1714-1768; Postow MA, et al. *N Engl J Med.* 2018;378:158-168.

ICI Pretreatment Evaluation

Routine Pretreatment Screening	
Clinical	• Physical examination. Comprehensive patient history of any autoimmune/ organ-specific disease, endocrinopathy, or infectious disease • Neurologic examination • Bowel habits (typical frequency/ consistency)
Imaging	• CT imaging • Brain MRI if indicated
General bloodwork	• CBC with differential • Comprehensive metabolic panel • Infectious disease screening as indicated
Dermatologic	• Examination of skin and mucosa if history of immune-related skin disorder

Routine Pretreatment Screening (cont'd)	
Adrenal/Pituitary/ Thyroid	• Serum cortisol • TSH, free T4
Pulmonary	• Oxygen saturation (resting and with ambulation) • Pulmonary function tests (PFTs) for high-risk patients
Cardiovascular	• Individualized assessment in consultation with cardiology as indicated
Musculoskeletal	• Joint examination/functional assessment as needed for patients with pre–existing disease

MRI = magnetic resonance imaging; TSH = thyroid stimulating hormone

National Comprehensive Cancer Network (NCCN Guidelines®). Management of Immunotherapy-Related Toxicities. Version 1.2019

Patient Monitoring and Evaluation

System	irAE	Signs/Symptoms
GI	Colitis	Diarrhea, increase in frequency of BM, abdominal pain, blood/mucus in stools, dark/tarry stools, severe abdominal pain/tenderness, ileus
Hepatic	Hepatitis	Abnormal LFTs/bilirubin, yellowing of eyes, dark urine, easy bruising/bleeding, severe N/v, right sided abdominal pain, drowsiness, diminished appetite
Skin	Dermatitis	Pruritus, rash, skin changes
Neuro	Neuropathies	Uni/bilateral weakness, paresthesias, sensory alterations
Endocrine	Endocrinopathies (thyroid, adrenal, pituitary, pancreas)	Unusual headaches, extreme fatigue, changes in mental status, mood or behavior, dizziness, fainting, hair loss, cold intolerance, deepening of voice, changes in weight, rapid heart rate, increased sweating, abdominal pain, low BP, abnormal thyroid tests or serum chemistries/enzymes
Pulmonary	Pneumonitis	Radiographic changes, new or worsening cough/shortness of breath, chest pain
Renal	Nephritis/renal dysfunction	Increase in serum creatinine, decrease in urinary output, hematuria, pedal edema, loss of appetite
Other		Changes in vision, eye inflammation, severe/persistent muscle/joint pain, severe weakness, changes in other laboratory values (CBC, PT/INR)

BM = bowel movement; BP = blood pressure; GI = gastrointestinal; INR = international normalized ratio; LFTs = liver function tests; N/V = nausea/vomiting; PT = prothrombin time

Brahmer JR, et al. *J Clin Oncol*. 2018;36(17):1714-1768; Postow MA, et al. *N Engl J Med.* 2018;378:158-168; National Comprehensive Cancer Network (NCCN Guidelines®). Management of Immunotherapy-Related toxicities. Version 1.2019

ASCO/NCCN 2019 Guidelines for Managing irAEs

Toxicity Grade	Recommendation
Grade 1	Continue checkpoint inhibitors with close monitoring, with exception of some neurologic, hematologic, and cardiac toxicities
Grade 2	Hold for most Grade 2 toxicities and consider resuming when symptoms and/or laboratory values return to Grade 1 or less Corticosteroids (initial dose of 0.5 to 1 mg/kg/d of prednisone or equivalent) may be given
Grade 3	Hold checkpoint inhibitors for Grade 3 AEs and initiate high-dose corticosteroids (prednisone 1 to 2 mg/kg/d or methylprednisolone IV 1 to 2 mg/kg/d) • Taper corticosteroids over course of at least 4 to 6 weeks • If symptoms do not improve with 48 to 72 hours of high-dose corticosteroid, infliximab may be offered for some toxicities
Grade 4	Warrants permanent discontinuation of checkpoint inhibitors, with exception of endocrinopathies controlled by hormone replacement

ASCO = American Society of Clinical Oncology

Brahmer JR, et al. *J Clin Oncol.* 2018;36(17):1714-1768; Postow MA, et al. *N Engl J Med.* 2018;378:158-168.

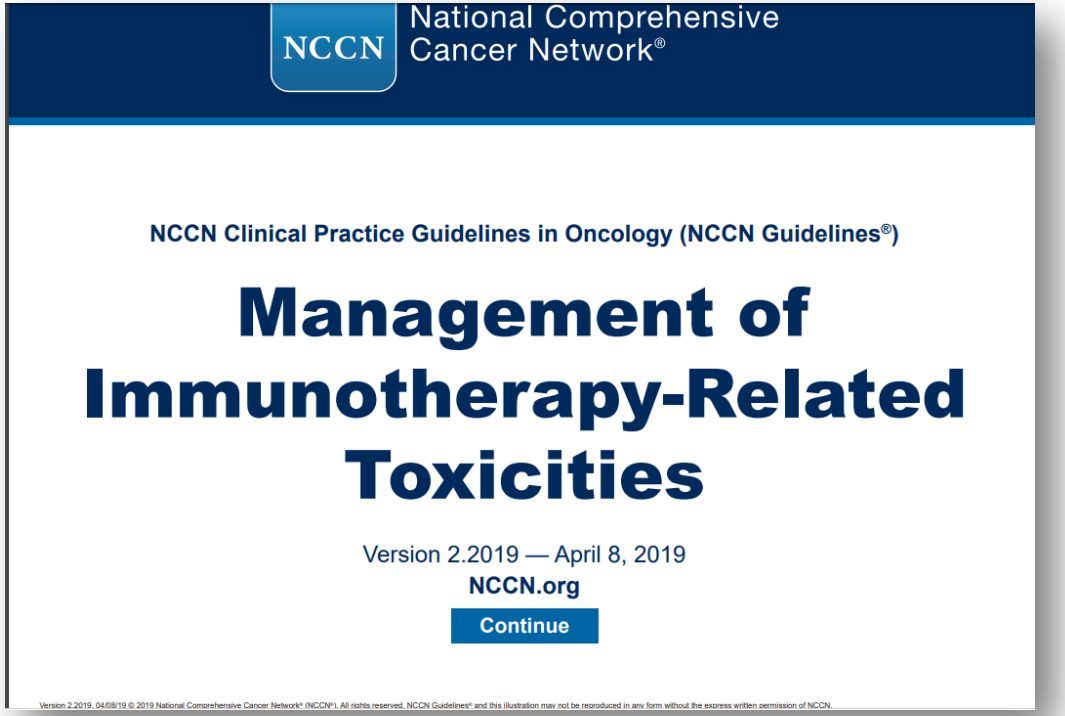
Principles of Steroid Immunosuppression

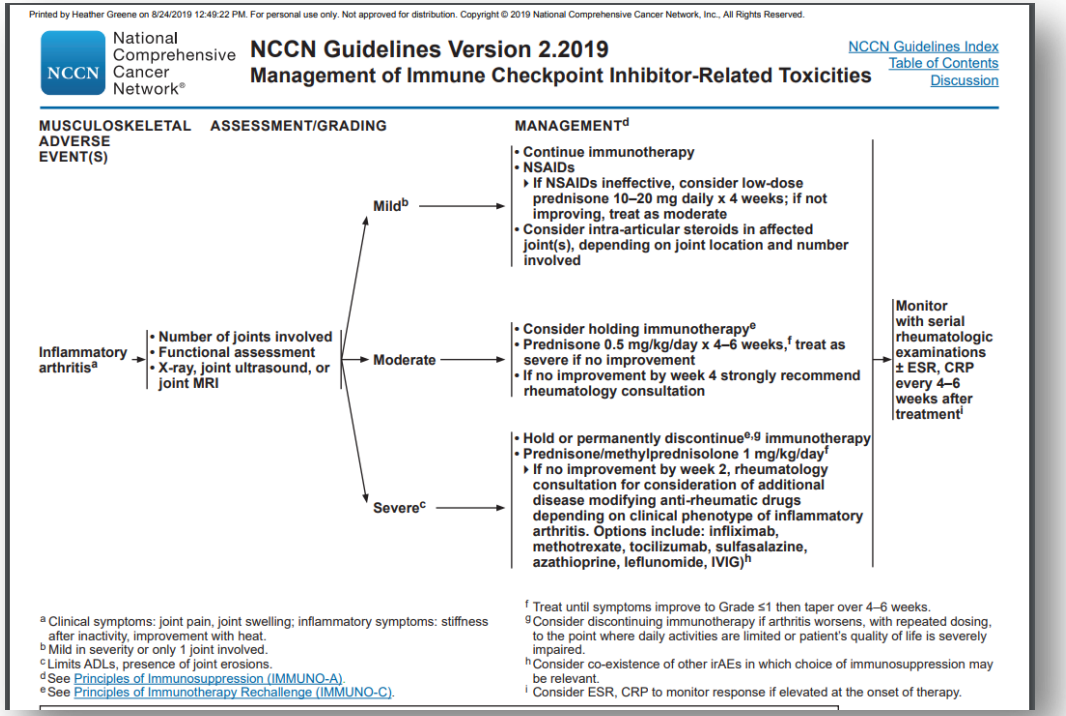
- Corticosteroids have not shown to decrease the antitumor effect of ICI therapy
  - But not recommended for pretreatment/prophylaxis prior to treatment
- GI prophylaxis
- Consider clotrimazole for thrush prevention
- PCP prophylaxis if on prednisone 20 mg/day >4 weeks, fluconazole if 6-8 weeks
  - Bactrim DS 1 PO every day
  - Zoster?
- Taper steroids over 4-6 weeks
  - Neuro, cardiac, and any grade 3/4 irAEs require methylprednisolone or higher dose prednisone 1-2 mg/kg/day
  - Higher dose topicals preferred over lower dose systemic steroids for dermatitis
- Endocrine irAEs may not need corticosteroid therapy → hormone replacement
- Steroid refractory: tumor necrosis factor alpha antagonists (infliximab) or mycophenalate (hepatitis)

PCP = pneumocystis pneumonia

O'Kane GM, et al. *Oncologist.* 2017;2270-80; National Comprehensive Cancer Network (NCCN Guidelines®). Management of Immunotherapy-Related toxicities. Version 1.2019; Weber JS, et al. *J Clin Oncol.* 2012;30:2691-7; Haanen JBAG, et al. *Ann Oncol*. 2017;28(suppl 4): iv119-iv142.

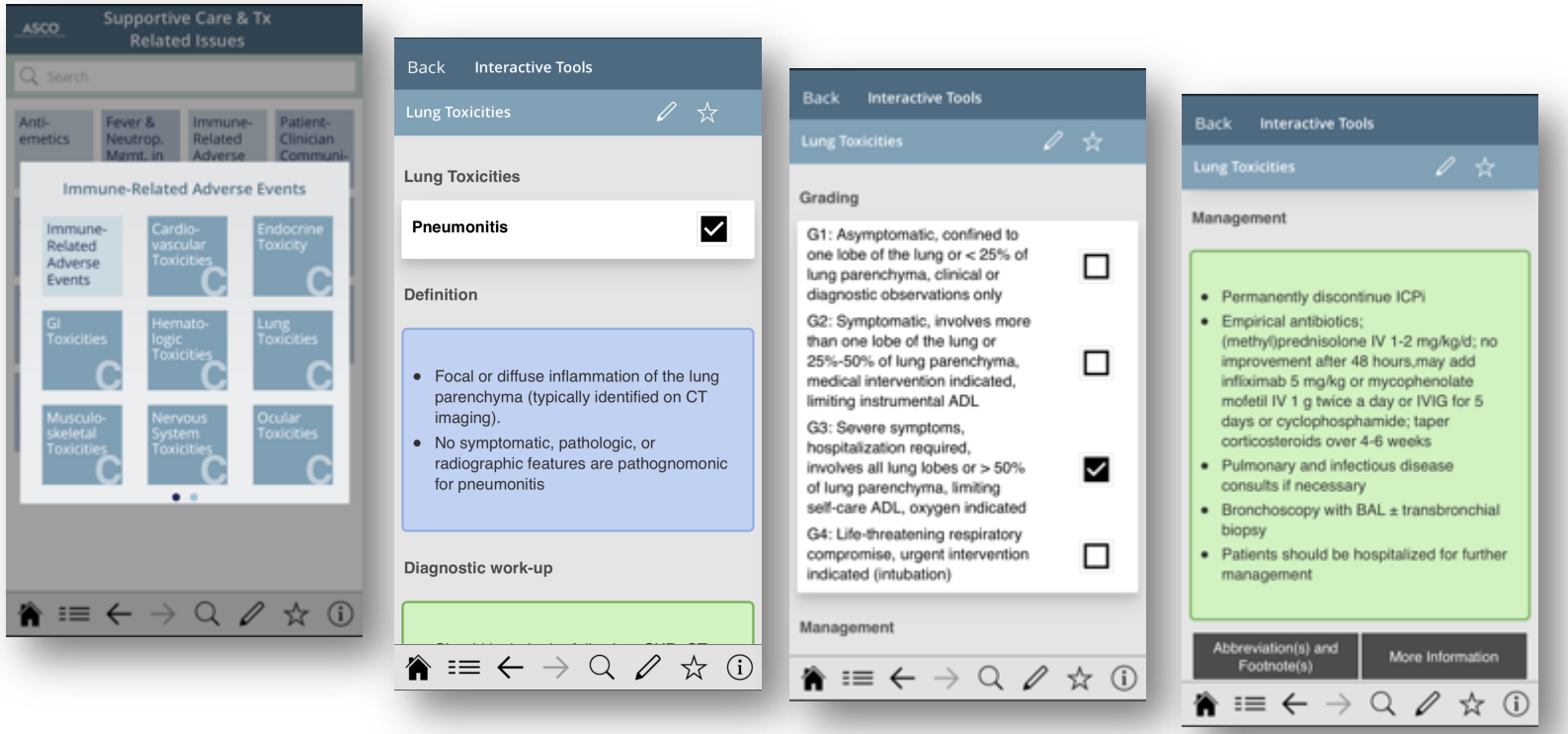
APP Resources: NCCN Guidelines



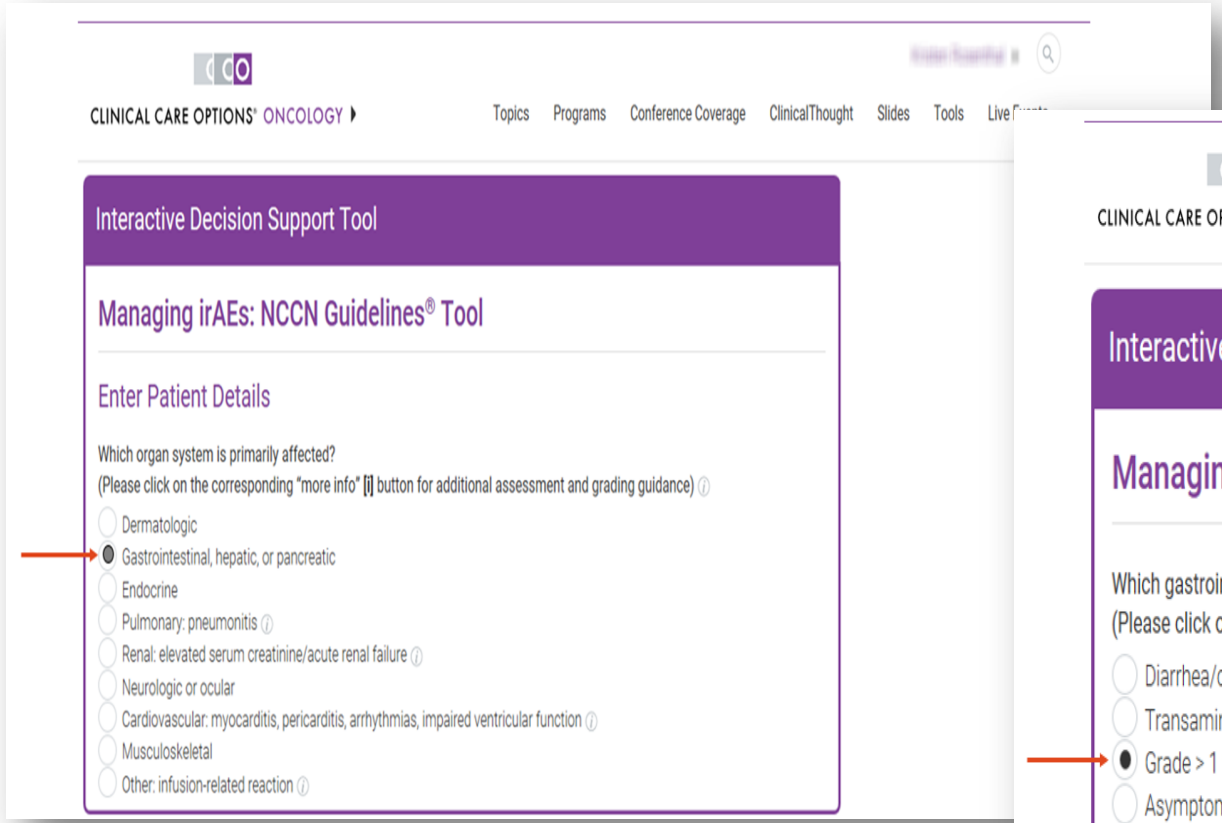


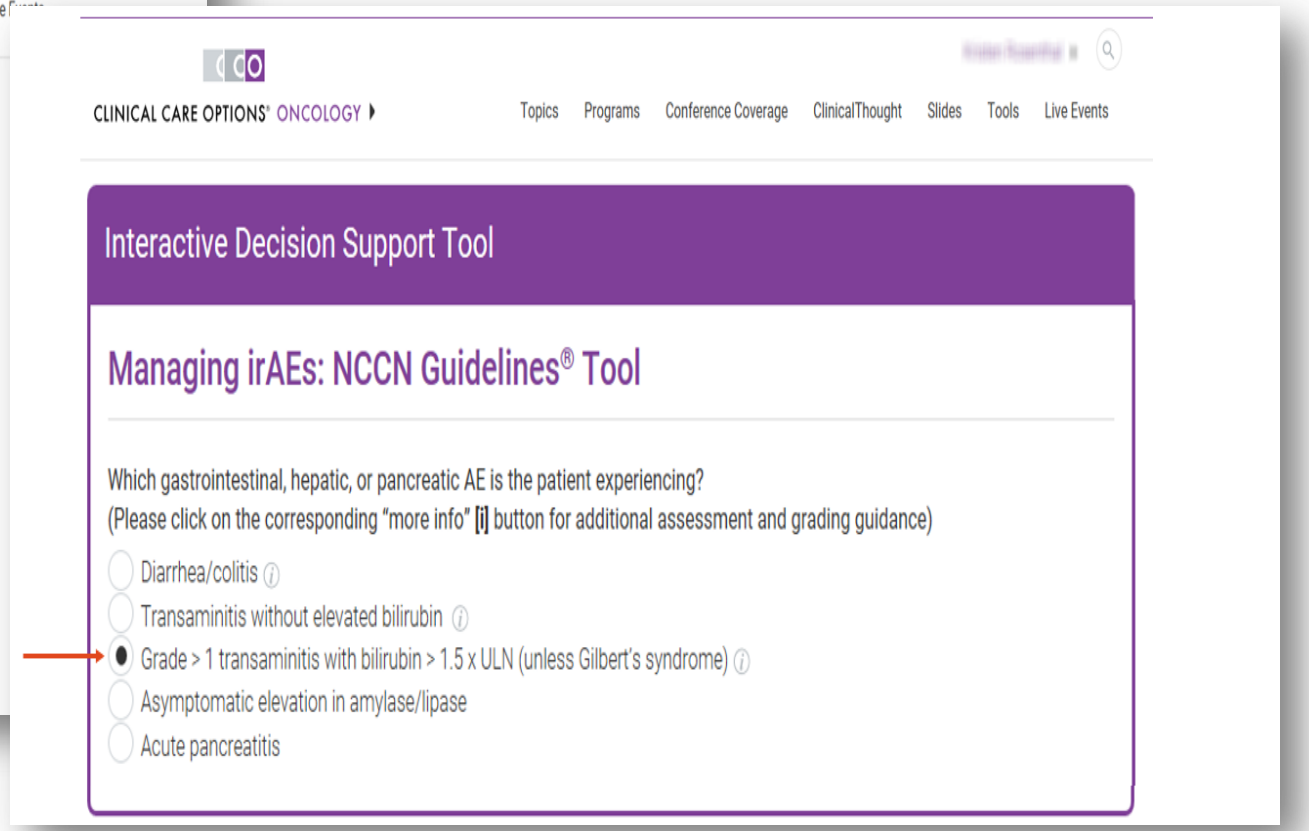
National Comprehensive Cancer Network (NCCN Guidelines®). Management of Immunotherapy-Related Toxicities. Version 1.2019.

Resources/Tools for irAE Management



Resources/Tools for irAE Management

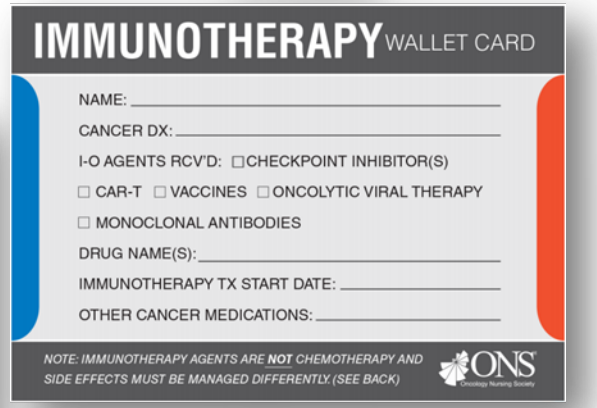




www.clinicaloptions.com/immuneAEtool

Patient Resources

Front



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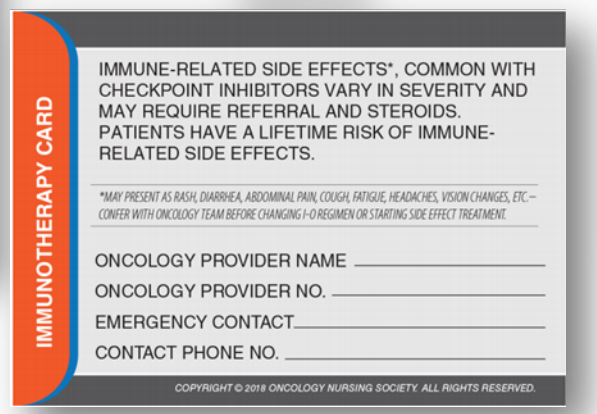


Association of Community Cancer Centers. https://www.accc-cancer.org/home/learn/immunotherapy/resource-detail/publication-io-wallet-card; Oncology Nursing Society, 2018, https://www.ons.org/sites/default/files/2019- 01/IO%20Card%201-sided_Vertical.pdf; Society for Immunotherapy of Cancer, 2019, https://www.sitcancer.org/connectedold/p/patient#resources

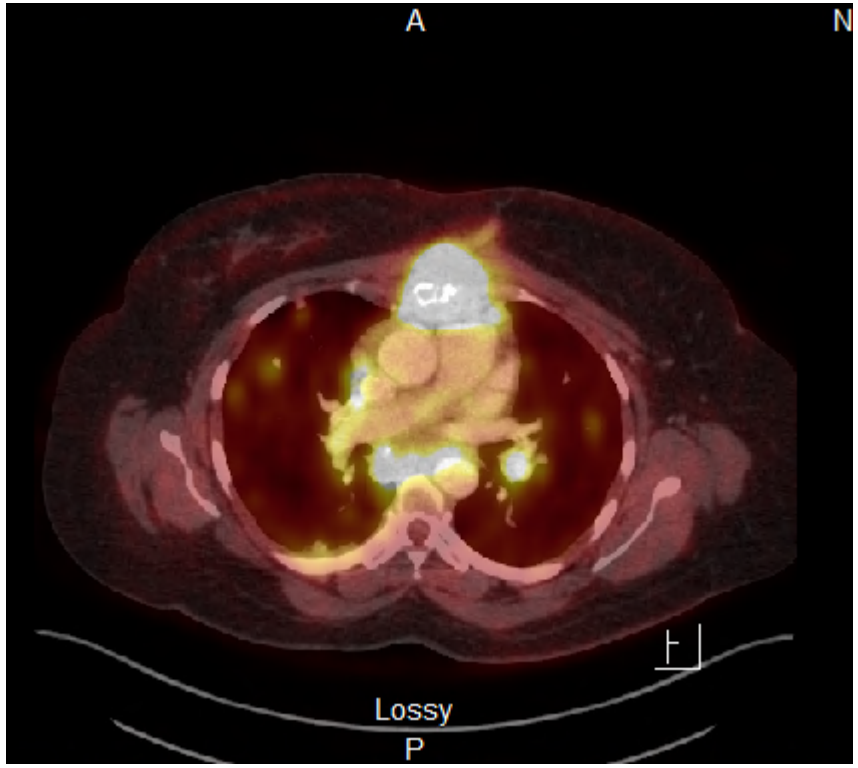
Case Study 2

- 62-year-old female, ECOG PS 1
- PMH: bipolar depression, hypertension, osteoarthritis
- T1cN0 1.8 cm, grade 3, IDC, ER-/PR-/HER2- s/p partial mastectomy, APBI and adjuvant chemo (TC x 4) in 2013
- Lost to follow-up
- June 2019 → presented to outside hospital with pleuritic chest pain
- CT chest showed numerous bilateral pulmonary nodules and sternal metastasis with cortical breakthrough and 3.1 x 3.4-cm soft tissue component

APBI = accelerated partial breast irradiation

Case Study 2

- PET scan July 2019: 4.5 x 4.1-cm destructive sternal mass, bilat pulmonary lesions, left axillary, left subpectoral, mediastinal, right hilar, retrocaval/pretracheal, AP window, subcarinal, AZ recess adenopathy; minimal portacaval lymph nodes



AP = aortopulmonary; AZ = azygoesophageal

Case Study 2

- Biopsy of parasternal mass
  - Metastatic breast cancer
  - ER-/PR-/HER2-

CANCER TYPE RELEVANT BIOMARKERS

Biomarker	Method	Result
MSI	NGS	Indeterminate
Mismatch Repair Status		Proficient
NTRK1	RNA-Seq	Fusion Not Detected
NTRK2	RNA-Seq	Fusion Not Detected
NTRK3	RNA-Seq	Fusion Not Detected
Tumor Mutational Burden		Intermediate | 9 Mutations/Mb
AKT1	NGS	Mutation Not Detected

CANCER TYPE RELEVANT BIOMARKERS (cont)

Biomarker	Method	Result
BRCA1	NGS	Mutation Not Detected
BRCA2	NGS	Mutation Not Detected
ERBB2 (Her2/Neu)	NGS	Mutation Not Detected
ESR1	NGS	Mutation Not Detected
PIK3CA	NGS	Mutation Not Detected
PTEN	IHC	Positive | 2+, 100%
	NGS	Mutation Not Detected

BIOMARKER	METHOD	RESULT	THERAPY ASSOCIATION		BIOMARKER LEVEL*
PD-L1 (SP142)	**IHC**	**Positive, IC: 5%**	**BENEFIT**	**atezolizumab + nab-paclitaxel**	**Level 1**
ER	IHC	Negative | 0	LACK OF BENEFIT	endocrine therapy	Level 1
ERBB2 (Her2/Neu)	IHC	Negative | 0	LACK OF BENEFIT	ado-trastuzumab emtansine (T-DM1), lapatinib, neratinib, pertuzumab, trastuzumab	Level 1
PR	IHC	Negative | 0	LACK OF BENEFIT	endocrine therapy	Level 1
AR	IHC	Negative | 0	LACK OF BENEFIT	bicalutamide, enzalutamide	Level 3A

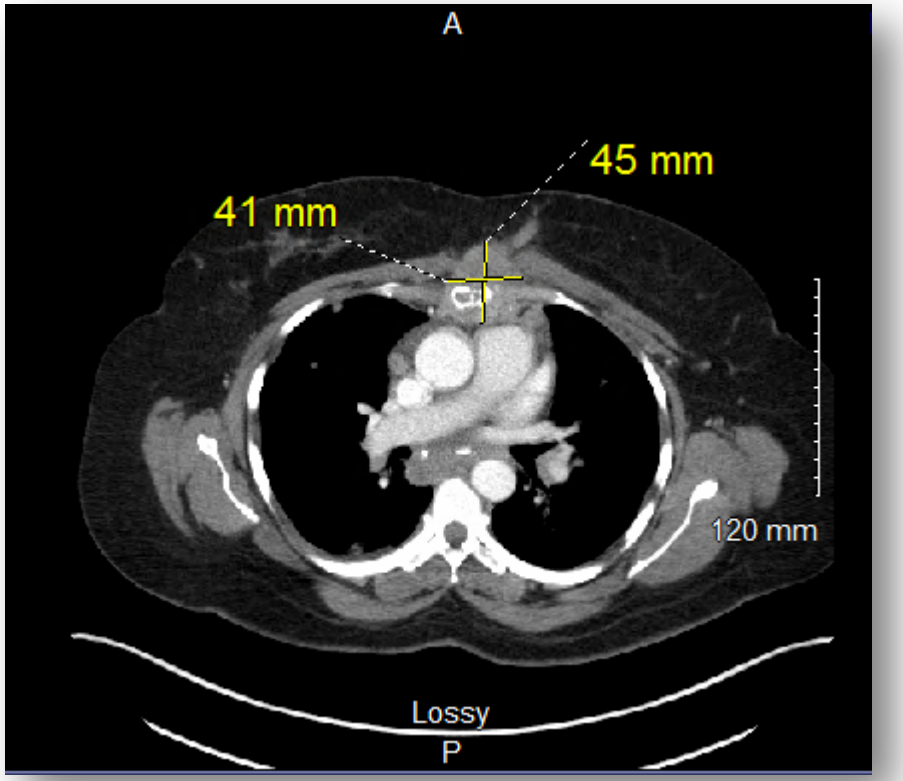
Case Study 2

- Started atezolizumab 840 mg IV days 1 and 15 + nab-paclitaxel 100 mg/m^2 IV days 1, 8, 15 every 28 days
- Baseline labs
  - Amylase 100
  - Lipase 61
  - TSH 0.631
  - CBC and CMP WNL
- C4D1 labs
  - Amylase 260
  - Lipase 81
  - TSH 0.956
  - Hgb 11.8
  - Hct 35%
  - WBC 3.5
  - ANC 1900
- CT CAP October 2019: significant response to therapy; no evidence of pancreatitis
- Clinically no abdominal pain or N/V (no ETOH)

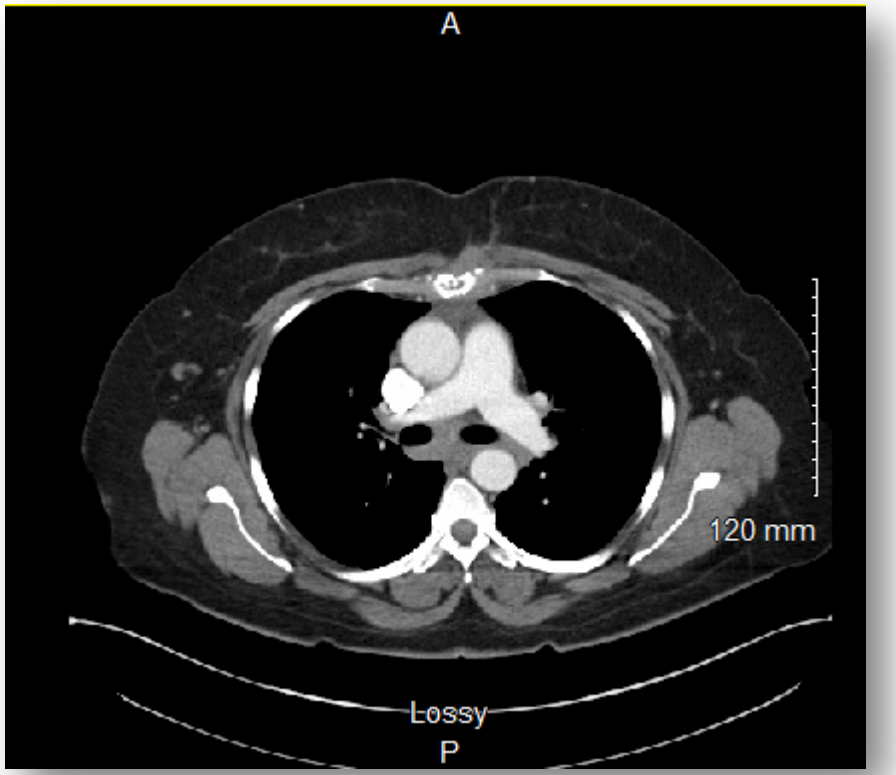
CAP = chest abdomen pelvis; CMP = comprehensive metabolic panel; Hct = hematocrit; WBC = white blood cell count; WNL = within normal limits

Case Study 2

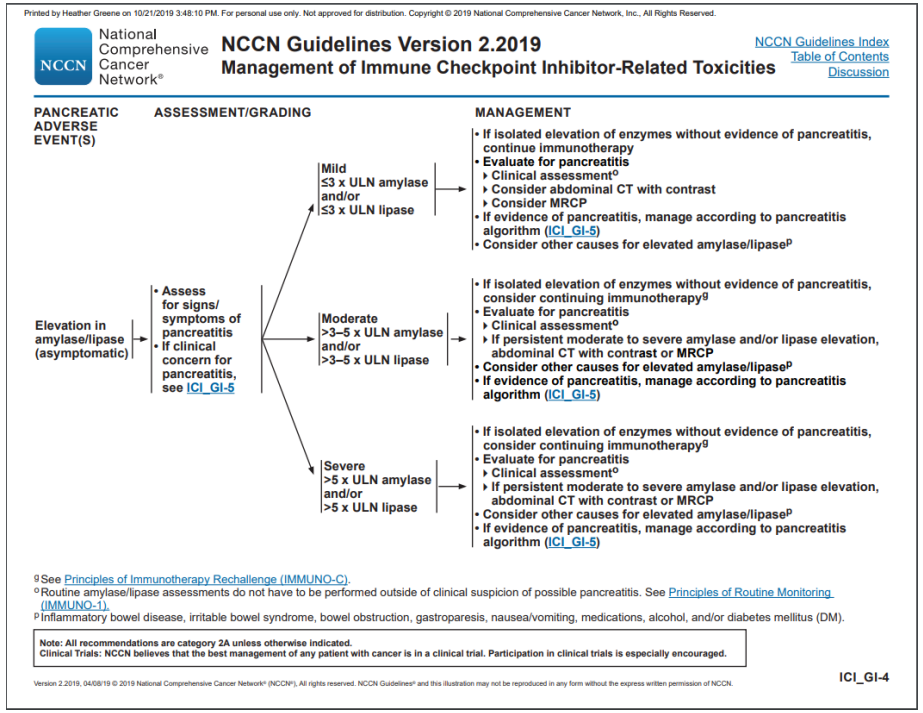
July 2019



October 2019



Case Study 2



- Elevated pancreatic enzymes, but **not** >3x ULN
- No clinical or radiographic evidence of pancreatitis
- Continue treatment and continue to monitor
- Advised to call physician's office with any abdominal pain, N/V

ULN = upper limit of normal

irAEs Associated With ICIs and Management Strategies: Key Takeaways

- APPs play a unique role in educating patients/caregivers about immunotherapy toxicities and management
- Side effects may develop up to 1 year after D/C
  - Patients may have moved on to next line of therapy
- Maintain a high level of suspicion when new symptoms appear
- Providers beyond the oncology team must be made aware of the potential for irAEs
  - Patients, caregivers, consultants, primary care providers, ED providers

APPs = advanced practice providers; ED = emergency department

Key Takeaways

- Current standards of care for TNBC can be optimized to provide improved outcomes for patients.
- The TNBC treatment landscape continues to evolve with many newly approved and emerging therapies, including ICIs plus chemotherapy for PD-L1+ disease, PARP inhibitors for g*BRCA*+ disease, and sacituzumab govitecan for heavily pretreated TNBC.
- APPs must understand how to identify and manage adverse events associated with these new and emerging therapies, including monitoring CBC for patients on PARP inhibitors, knowing that ICI AEs can develop up to 1 year after therapy discontinuation, and utilizing dose interruptions, modifications, and delays to ensure the best treatment outcomes

Expert Insights on Triple-Negative Breast Cancer: Preparing for the Next Wave of Treatments

Thank you for joining us!

Please complete your evaluation.