Immunotherapy in Breast Cancer

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Overview

- Rationale for immunotherapy (IO) in TNBC and combination with chemotherapy
- Metastatic TNBC: Current state of IO & PD-L1 as biomarker
- Early TNBC: Current state of IO & PD-L1 as biomarker
- Patient perspective: PRO in IO trials of early and advanced TNBC
- Conclusions and future directions

Rationale for IO in TNBC and Combination with Chemotherapy

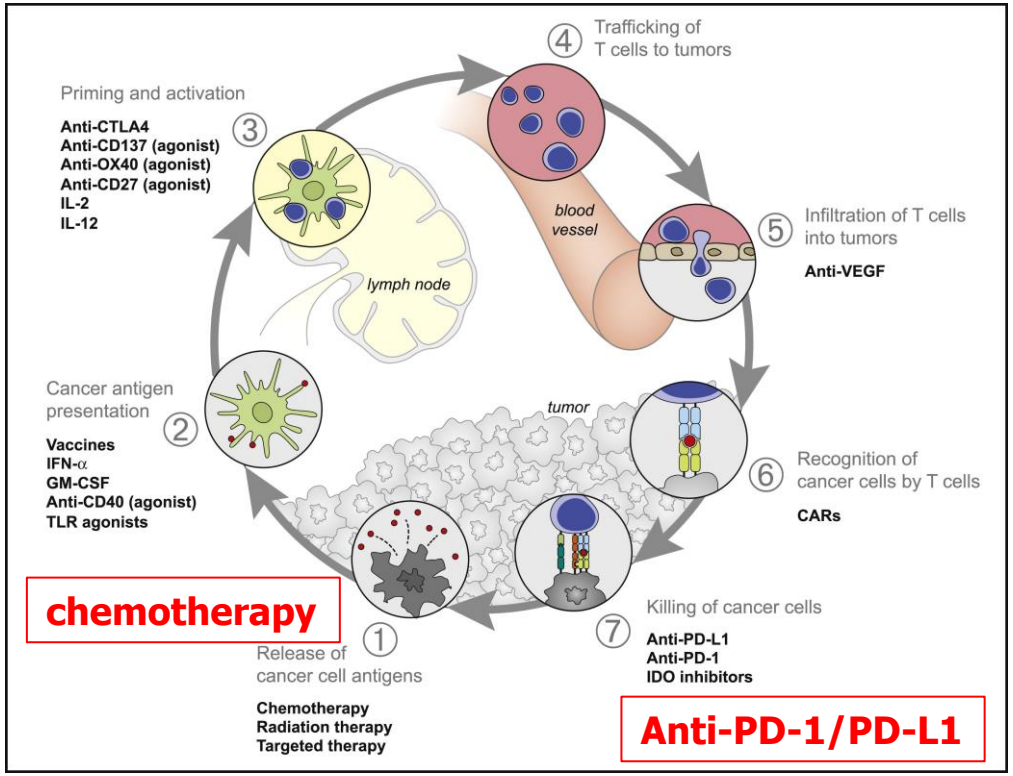
Immune checkpoints in breast cancer

- Expression associated with tumor-infiltrating lymphocytes (TILs)
- TILs are evidence of anti-tumor immune response; highest in TNBC
- **PD-L1** expressed mainly in infiltrating immune cells in BC
- **PD-1** on T-cells down-regulates immune response, blocking PD-1/PD-L1 can augment T-cell response

Anti- PD-1/PD-L1 antibodies have shown single agent activity in TNBC including durable responses (1L > 2L+)

Combination of IO with cytotoxics

- Chemotherapy is SOC in TNBC and can have several immunogenic effects, TIL-rich tumors have highest pCR rates
- Combination with chemotherapy may be synergistic by targeting different steps in the cancer immunity cycle
- Nab-paclitaxel – rational partner as no steroid requirement



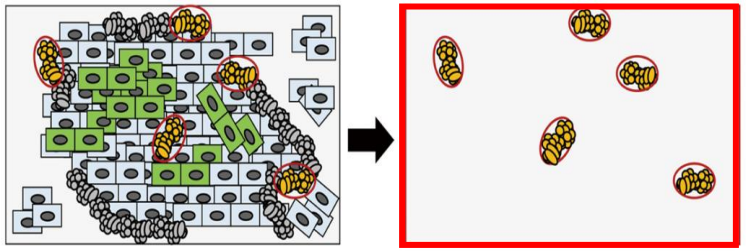
Luen et al, Breast 2016, Stanton et al, Jama Onc 2016, Nanda et al, JCO 2016, Adams et al Ann Oncol 2019, Cortes et al, ESMO 2019, Emens et al, JAMA Onc 2019, Gatti-Mays et al, Nature Breast Cancer 2019, Loi et al, JCO 2019, Adams et al, JAMA Onc 2019, Denkert et al, Lancet Oncol 2018, Page et al, Nature Breast Cancer 2019, Galluzzi et al, Nat Rev Clin Oncol 2020, Chen/Mellman Immunity 2013

Metastatic

- Keynote 355
- Impassion 130

PD-L1 as Biomarker (in metastatic setting)

Two different PD-L1 companion diagnostics approved in US



Score	IHC Assay	Grading	FDA Indication mTNBC
Immune cell score (IC)	Ventana SP142	% of tumor area covered by area of PD-L1+ immune cells	Atezolizumab **(IC ≥ 1%)** 41% in IMpassion130
Combined positive score (CPS)	Dako 22c3	Total number of PD-L1–positive cells (tumor cells, lymphocytes, and macrophages) divided by the total number of tumor cells x 100	Pembrolizumab **(CPS ≥ 10)** 37% in KEYNOTE-355

Retrospective comparison of SP142 and 22c3 assays in IMpassion130 (biomarker evaluable = 614 pts):
Rates of PD-L1 positivity vary by assay and threshold, analytic and clinical concordance suboptimal, clinical dilemma (see commentary Salgado et al, Lancet Oncol 2020)

Rugo et al ESMO 2019, Rugo et al SABCS 2019
Figure modified from Eckstein et al, Ann Transl Med 2019

Phase 3 IO chemo combination 1L advanced TNBC-KN-355

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

R 2:1

- Pembrolizumab[a] + Chemotherapy[b]
- Placebo[c] + Chemotherapy[b]

Progressive disease[d]/cessation of study therapy

Chemotherapy regimens:
- Nab-paclitaxel (31%)
- Paclitaxel (13%)
- Gemcitabine/carboplatin (55%)

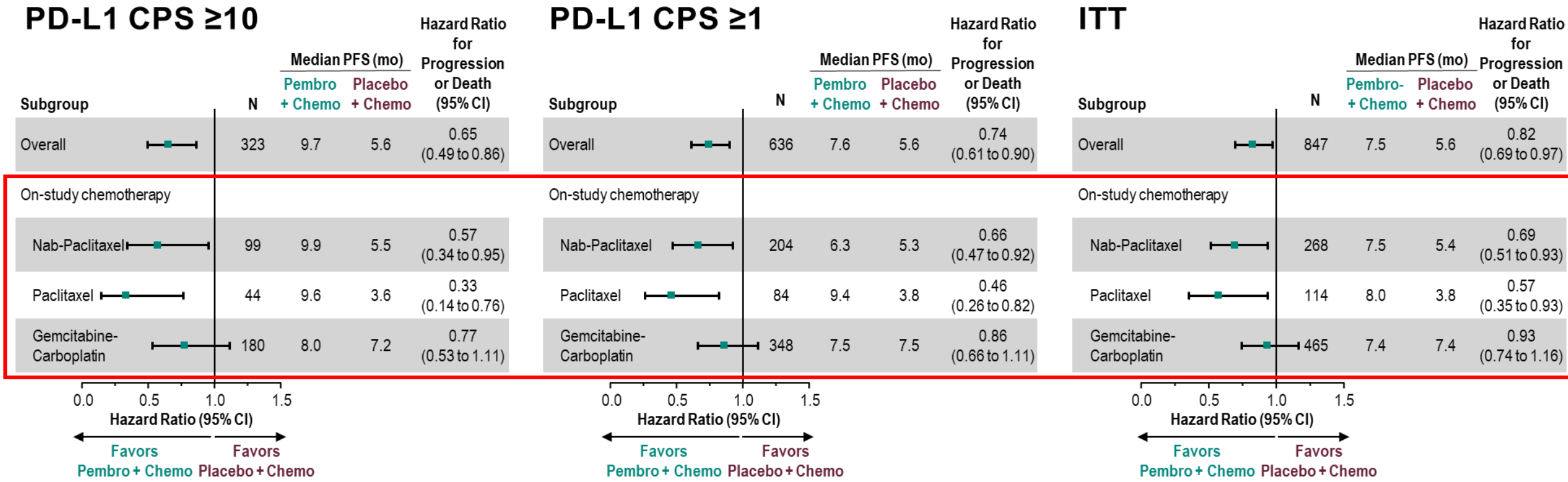
Stratification Factors:
- Chemotherapy on study (taxane vs gemcitabine-carboplatin)
- PD-L1 tumor expression (CPS ≥1 vs CPS <1)[e]
- Prior treatment with same class chemotherapy in the neoadjuvant or adjuvant setting (yes vs no)

Efficacy endpoints
- Primary Endpoints
  - PFS in PD-L1+ (CPS ≥10 and CPS ≥1) and ITT
  - OS in PD-L1+ (CPS ≥10 and CPS ≥1) and ITT
- Secondary Endpoints
  - ORR, DCR, DOR
- Exploratory Endpoint
  - Consistency of treatment effect in all patients and PD-L1+ (CPS ≥10 and CPS ≥1) according to on-study chemotherapy partner

Cortes et al, ASCO 2020, Rugo et al, SABCS 2020

Phase 3 IO chemo combination 1L advanced TNBC-KN-355

Consistency of efficacy per chemo regimen^



^ exploratory, not powered

Cortes et al, ASCO 2020, Rugo et al, SABCS 2020

Phase 3 IO chemo combination 1L advanced TNBC-KN-355

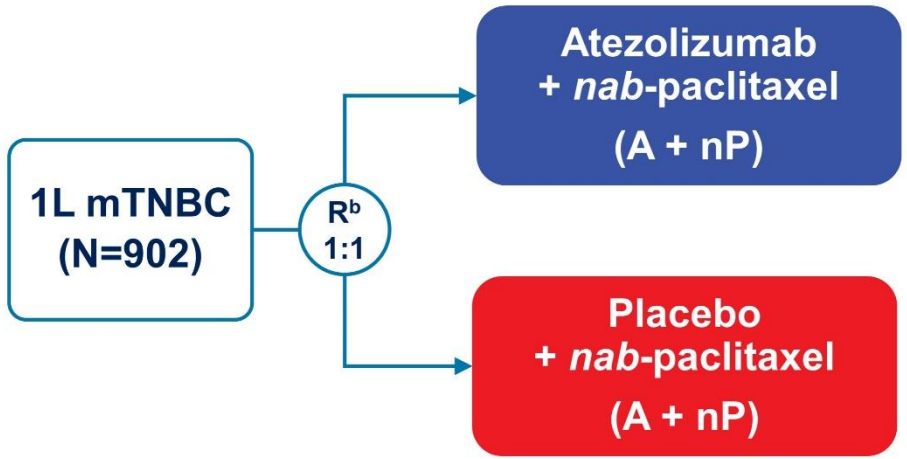
Secondary endpoints

Trial	Target	Chemo	N	Open (Estimated Completion)	PD-L1+	Primary endpoints (Hierarchical testing)	Secondary endpoints	De novo, DFI (mos)
KEYNOTE-355 (NCT02819518) FDA approval 11/2020	**PD-1**	**Nab-Paclitaxel** Or **paclitaxel** Or **gem/carbo**	847	July 2016 (Dec 2019)	CPS≥10 37% CPS≥1 75%	PFS CPS≥10 **9.7 vs 5.6 mos** PFS CPS≥1 7.6 vs 5.6 n.s.* PFS ITT 7.5 vs 5.6 n.t.* OS in PD-L1+ (pending) OS ITT (pending)	CPS≥10 | CPS≥1 | ITT **ORR (%):** 53 vs 40 | 45 vs 38 | 41 vs 36 **DCR (%):** 65 vs 54 | 59 vs 54 | 56 vs 52 **DOR (mos):** 19 vs 7 | 10 vs 7 | 10 vs 6	29%, ≥ 6

* By hierarchical testing (n.s. not significant, n.t. not tested)
^ exploratory, not powered

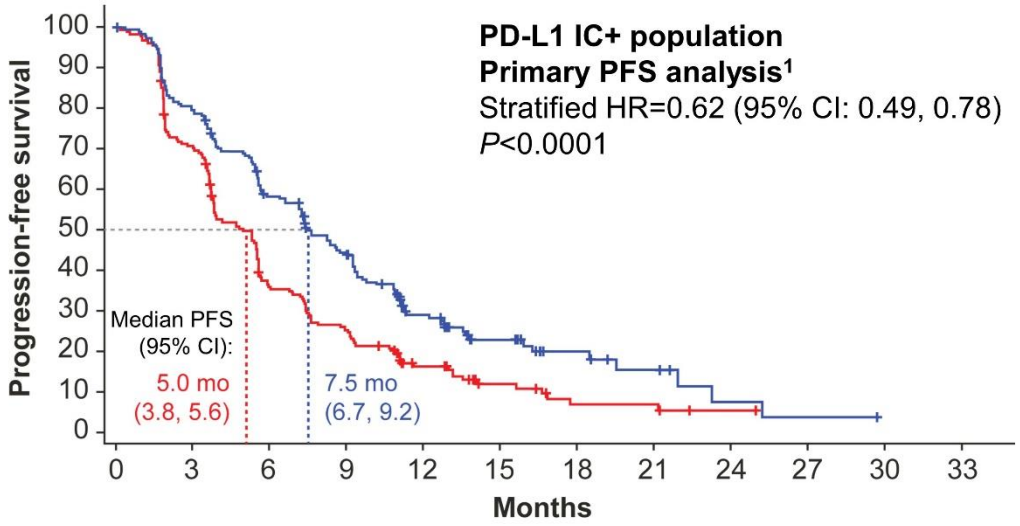
Cortes et al, ASCO 2020, Rugo et al, SABCS 2020

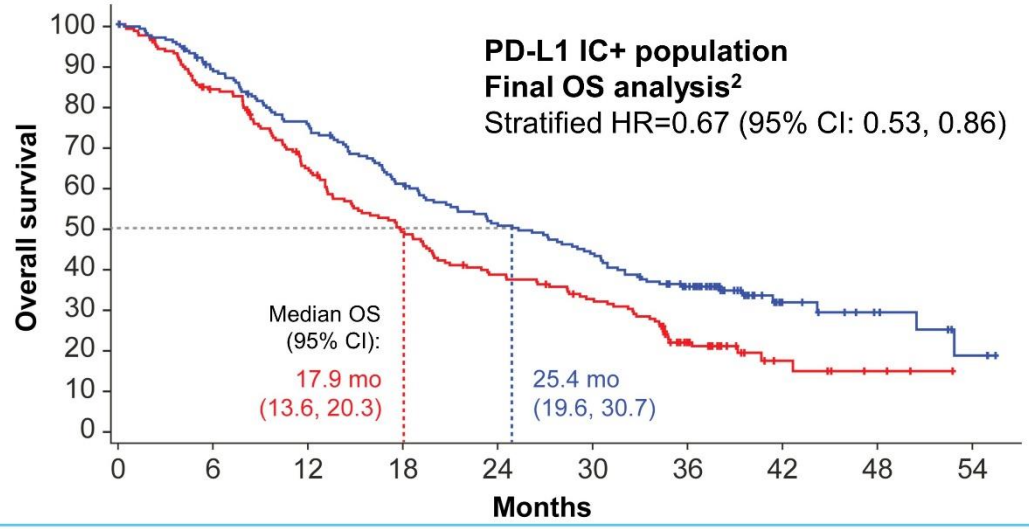
Phase III IMpassion130 study[a]



Co-primary endpoints:

- PFS (tested in parallel in the ITT and PD-L1 IC+ populations[c])
- OS (hierarchically tested in ITT and PD-L1 IC+ populations)

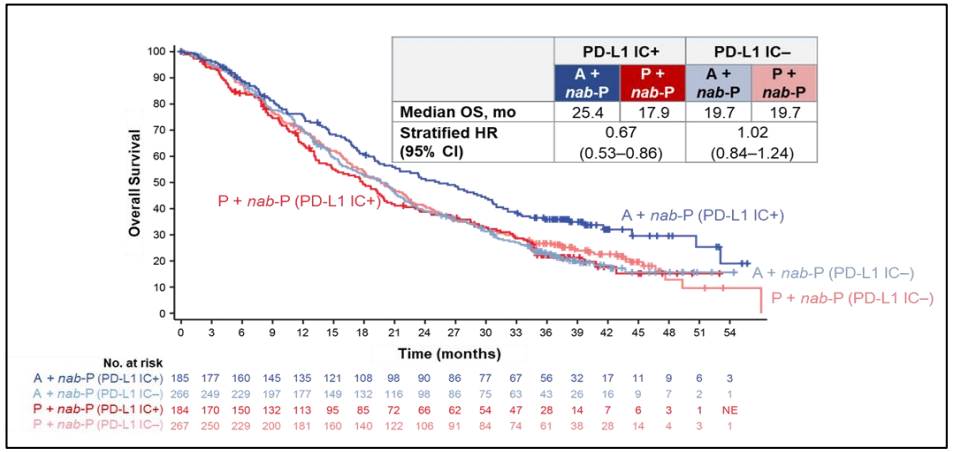


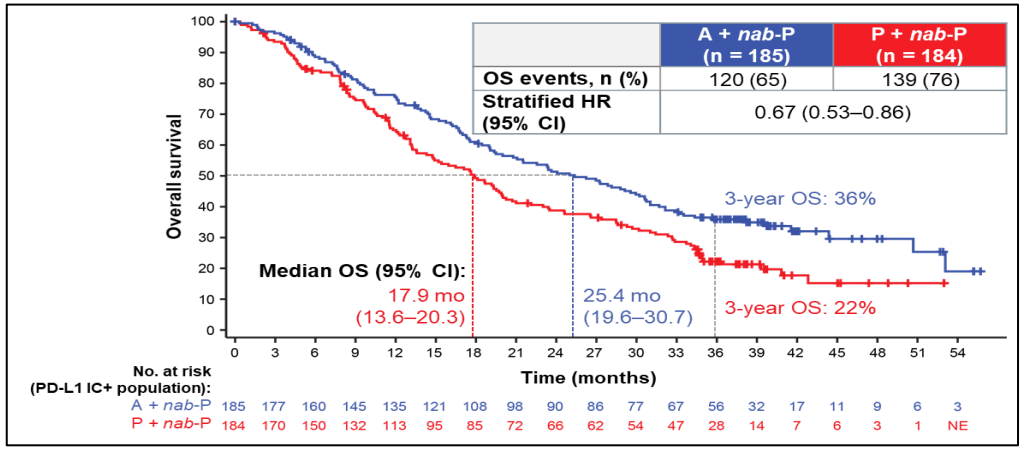


[a] ClinicalTrials.gov: NCT02425891. [b] Stratification factors: liver metastases, prior taxanes, PD-L1 IC status (VENTANA SP142 IHC assay). [c] PD-L1–expressing immune cells covering ≥1% of the tumor area.
1. Schmid P. NEJM 2018. 2. Emens L. ESMO 2020 [Abstract LBA16].

PD-L1 as Biomarker (in metastatic setting)

✓ PD-L1 predictive for IO benefit in mTNBC: OS in IMpassion130





✓ Degree of PD-L1 positivity correlates with efficacy of IO therapy in mTNBC

- Shown in pre-specified analyses of KN-355 (1L combination therapy)
- Demonstrated in exploratory analyses of KN-119 (2L monotherapy)

KEYNOTE 355	HR PFS Pembro/PLA	Duration of response Pembro arm
IIT	0.82	10.1 mos
CPS ≥ 1	0.74	10.1 mos
CPS ≥ 10	0.65	19.3 mos

KEYNOTE 119	Median OS Pembrolizumab arm
CPS ≥ 1	10.7 mos
CPS ≥ 10	12.7 mos
CPS ≥ 20	14.9 mos

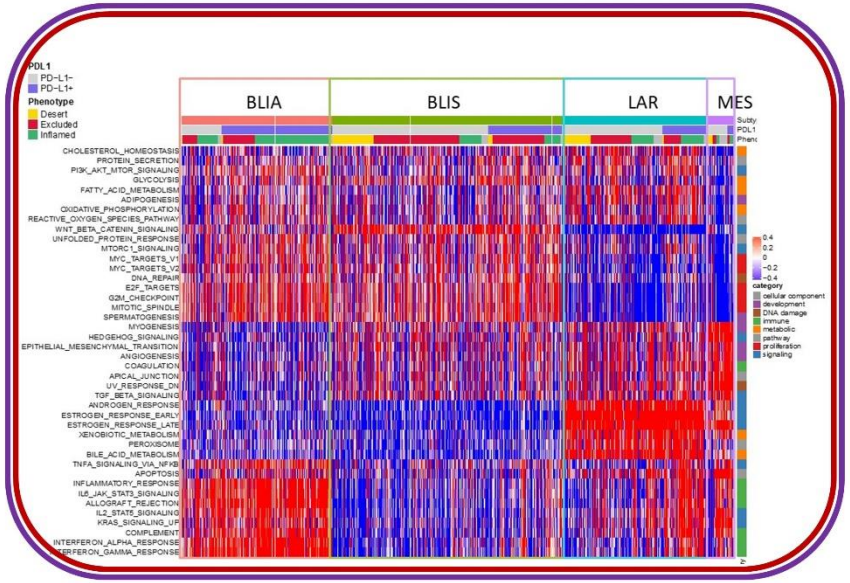
Emens et al, ESMO 2020, Cortes et al ESMO 2019, Cortes et al ASCO 2020

TME evaluation in IMpassion130

Immune phenotypes assessed according to the location of tumor/stroma CD8 by IHC

ITT population (N=902)

- PD-L1 IHC[1,2]
- sTILs[1]
- CD8 IHC[1] (n=802) → Immune phenotypes
- TMB[3]
- Genomic[4]
- RNA-Seq (n=836) → Molecular subtypes; GSEA hallmark pathways; Cellular deconvolution



Molecular subtypes were assessed with RNA-seq, using Burstein classification[5]

GSEA, gene set enrichment analysis.

1. Emens L. JNCI 2021.
2. Rugo H. ESMO 2019.
3. Emens L. ESMO 2020.
4. Emens L. SABCS 2020.
5. Burstein M. CCR 2015.

Safety of IO in metastatic TNBC

Organ-specific Immune-related Adverse Events in metastatic TNBC trials (n>1000 patients)

irAE		All grades (%)	Grade 3-4 (%)	Grade 5 (%)
Dermatologic	Pruritis, Rash	18	0.5	0
Endocrine	Hypothyroidism	12	0	0
	Hyperthyroidism	5	0.1	0
Gastro-intestinal	Hepatitis; elevated transaminases	10	3	0.2
	Colitis, diarrhea	2.5	0.45	0
Hematologic	Prespecified autoimmune anemia, lymphopenia, thrombocytopenia and clotting abnormalities	4	1	0.2
Respiratory	Pneumonitis	3	0.5	0.1
Other (<1%)	Adrenal insufficiency, type 1 diabetes, ocular, myositis, neurological/myositis, nephritis/elevated creatinine	<1	<0.5	0

irAE incidence in mTNBC (any grade)

- Single agent: 18.5%
- Higher in combination trials:
  - 57% atezolizumab+nab-pac
  - 42% nab-pac monotherapy

Management guidelines ASCO/NCCN

(Brahmer et al, J Clin Oncol 2018)

D'Abreo and Adams. Nat Rev Clin Oncol 2019

Phase 3 IO chemo combination 1L advanced TNBC trials

Trial	Target	Chemo	N	Open (Estimated Completion)	PD-L1+	Primary endpoints (Hierarchical testing)	Secondary endpoints	De novo, DFI (mos)
IMpassion130 (NCT02425891) FDA approval 3/2019	**PD-L1**	**Nab-Paclitaxel**	900	June 2015 (April 2020)	IC≥1 41%	PFS ITT **7.2 vs 5.5 mos** PFS PD-L1+ **7.5 vs 5 mos** OS ITT 21 vs 18.7 mos n.s.* OS PD-L1+ 25.4 vs 17.9 mos n.t.*	ITT | PD-L1+ **ORR (%):** 56 vs 46% | 59 vs 43% **DOR (mos)**: 7.4 vs 5.6 | 8.5 vs 5.5 **PRO** (no detriment to HRQoL with added IO)	37%, ≥ 12
IMpassion131 (NCT03125902) FDA warning	**PD-L1**	**Paclitaxel**	651	Aug 2017 (June 2021)	IC≥1 45%	PFS PD-L1+ 6 vs 5.7 mos n.s. PFS ITT 5.7 vs 5.6 mos n.t.*	PD-L1+ | ITT **OS (mos):** 22.1 vs 28.3 | 19.2 vs 22.8 ORR, PFS by IRC and PRO (pending)	30%, ≥ 12
IMpassion132 (NCT03371017)	**PD-L1**	**Gem/carbo** Or **capecitabine**	350	Jan 2018 (Jan 2021)	IC≥1 n/a	OS in PD-L1+ (pending) OS in ITT (pending)	12-mos OS, 18-mos OS, PFS, RR, DOR, CBR, PRO (pending)	0, ≤ 12
KEYNOTE-355 (NCT02819518) FDA approval 11/2020	**PD-1**	**Nab-Paclitaxel** Or **paclitaxel** Or **gem/carbo**	847	July 2016 (Dec 2019)	CPS≥10 37% CPS≥1 75%	PFS CPS≥10 **9.7 vs 5.6 mos** PFS CPS≥1 7.6 vs 5.6 n.s.* PFS ITT 7.5 vs 5.6 n.t.* OS in PD-L1+ (pending) OS ITT (pending)	CPS≥10 | CPS≥1 | ITT **ORR (%):** 53 vs 40 | 45 vs 38 | 41 vs 36 **DCR (%):** 65 vs 54 | 59 vs 54 | 56 vs 52 **DOR (mos):** 19 vs 7 | 10 vs 7 | 10 vs 6 Consistency of efficacy per chemo regimen^ **PFS HR nab-Pac:** 0.57 | 0.66 | 0.69 **PFS HR Pac:** 0.33 | 0.46 | 0.57 **PFS HR Gem/Carbo:** 0.77 | 0.86 | 0.93	29%, ≥ 6

IMpassion130: Atezolizumab 840/PLA q2w + Nab-Paclitaxel 100 D1, 8, 15 of 28 days
IMpassion131: Atezolizumab 840/PLA q2w + Paclitaxel 90 D1, 8, 15 of 28 days, 8–10 mg dexamethasone x at least 2 infusions. Stratifier prior taxane, PD-L1 status, liver mets, geographic location. 49% prior taxane, 50% prior anthracycline
IMpassion132: Atezolizumab 1200/PLA d1 q 3w + chemo (Gemcitabine 1000/carboplatin AUC 2 d 1, 8 of 21 days or Capecitabine 1000 mg/m2, BID d1 to 14 q21d)
KN-355: Pembro 200/PLA q3w + Chemo (Nab-Pac 100 D1, 8, 15 of 28 days Or Pac 90 D1, 8, 15 of 28 days Or Gem/ Carbo D1, 8 of 21 days). Stratified by taxane (45%) vs not (55%), PD-L1, prior expos to chemo class (same 22%).

* By hierarchical testing (n.s. not significant, n.t. not tested)
^ exploratory, not powered

Schmid et al, NEJM 2018, Adams et al, Ann Oncol 2020, Miles et al, ESMO 2020, Cortes et al, ASCO 2020, Rugo et al, SABCS 2020

Summary IO in advanced TNBC

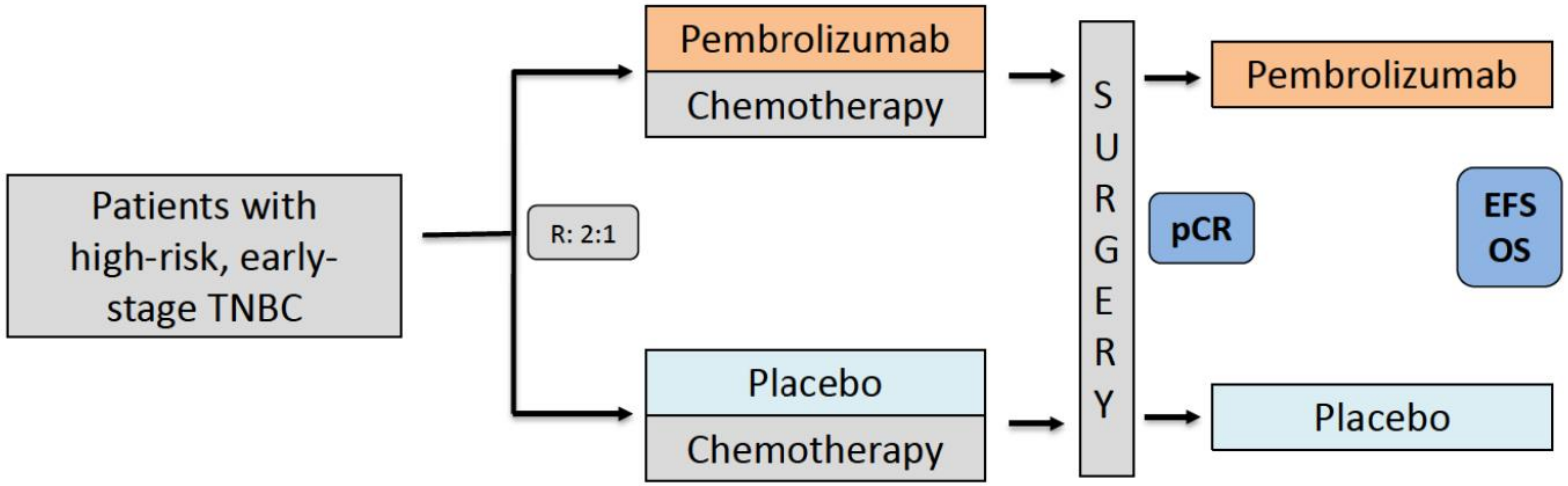
- Combining immune checkpoint inhibitors with chemotherapy has been demonstrated in two RPh3 trials to improve PFS. FDA approval for atezolizumab as well as pembrolizumab in PD-L1+ mTNBC.
- OS data appear promising.
- PD-L1 is an imperfect biomarker although the best to date. Degree of positivity associated with IO efficacy.
- Dilemma of different companion diagnostics and thresholds. Required hierarchical testing in trials and complicates clinical decision-making.
- Insufficient evidence of optimal chemotherapy backbone, trials not powered for comparison. Caution not to use paclitaxel with atezolizumab.
- Toxicity is manageable, PRO without detriment from added IO.

<u>Unmet needs & unanswered questions</u>

- De-escalation: Does every patient need chemotherapy? Who will do as well with IO monotherapy? Predictive markers?
- Effective therapies for PD-L1- mTNBC sorely needed
- Despite progress for PD-L1+ mTNBC, OS still too low

Neoadjuvant

Keynote 522 study schema



Co-primary endpoints: pCR rate and EFS

Key secondary endpoint: OS

Chemo= paclitaxel/carbo→AC Q3 wks x 4
Pembro continued Q3wks adjuvantly x 9 cycles

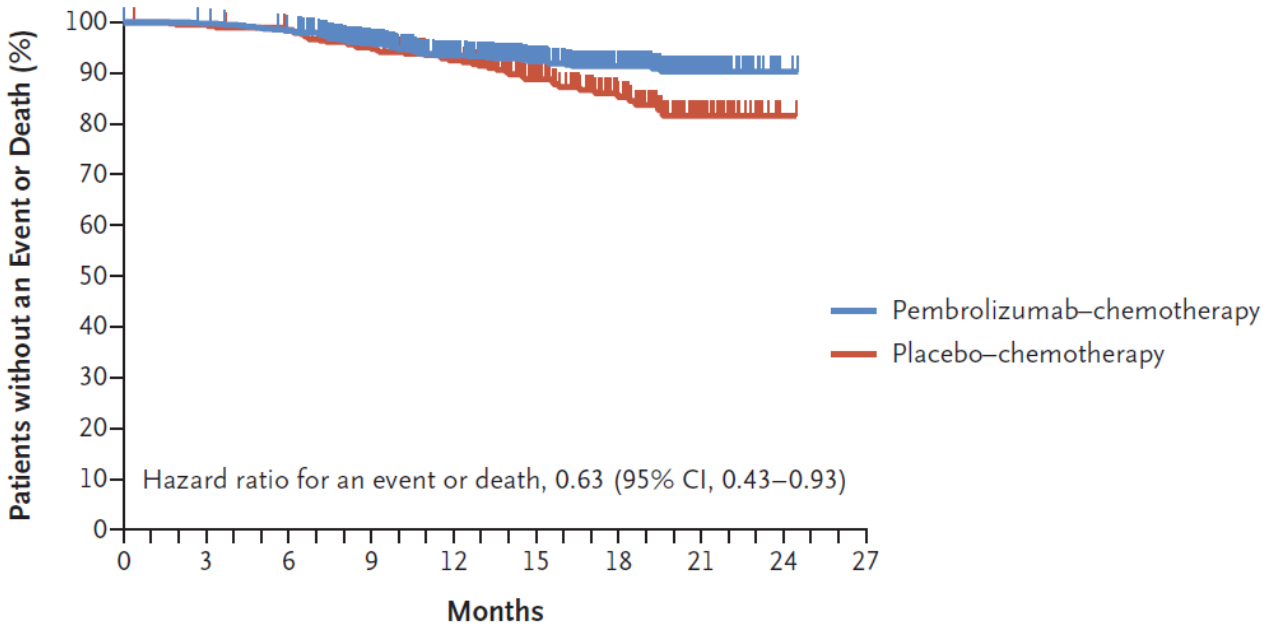
Keynote 522: pCR

Table 2. Pathological Complete Response, According to Pathological Stage.*

Variable	Pembrolizumab–Chemotherapy (N = 401)	Placebo–Chemotherapy (N = 201)	Estimated Treatment Difference¡	P Value
			percentage points (95% CI)	
Pathological stage ypT0/Tis ypN0				
No. of patients	260	103		
Percentage of patients with response (95% CI)	64.8 (59.9–69.5)	51.2 (44.1–58.3)	13.6 (5.4–21.8)	P<0.001
Pathological stage ypT0 ypN0				
No. of patients	240	91		
Percentage of patients with response (95% CI)	59.9 (54.9–64.7)	45.3 (38.3–52.4)	14.5 (6.2–22.7)	
Pathological stage ypT0/Tis				
No. of patients	275	108		
Percentage of patients with response (95% CI)	68.6 (63.8–73.1)	53.7 (46.6–60.8)	14.8 (6.8–23.0)	

P Schmid et al *N Engl J Med* 2020;382:810-21.

Keynote 522: Event Free Survival (EVS)

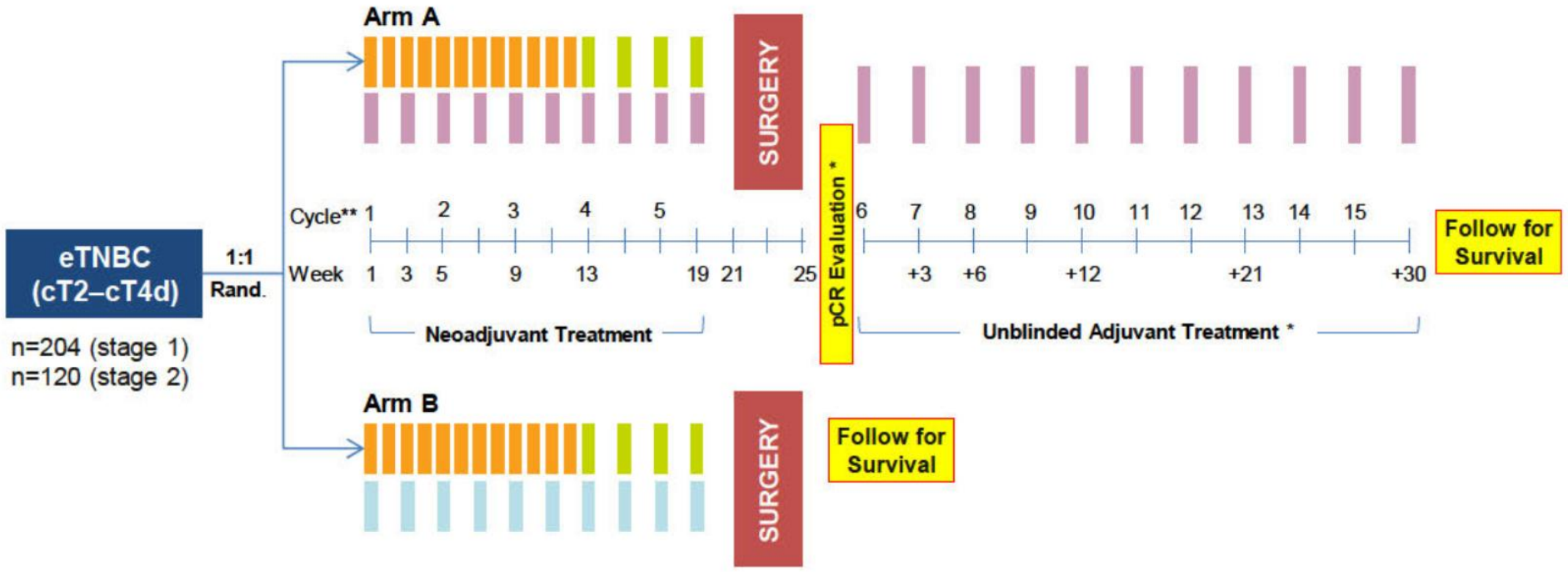


No. at Risk										
Pembrolizumab–chemotherapy	784	780	765	666	519	376	242	73	2	0
Placebo–chemotherapy	390	386	380	337	264	186	116	35	1	0

EVS: “Progression of disease that precludes surgery, local or distant recurrence, second primary malignancy (breast or other cancers) or death due to any cause.”

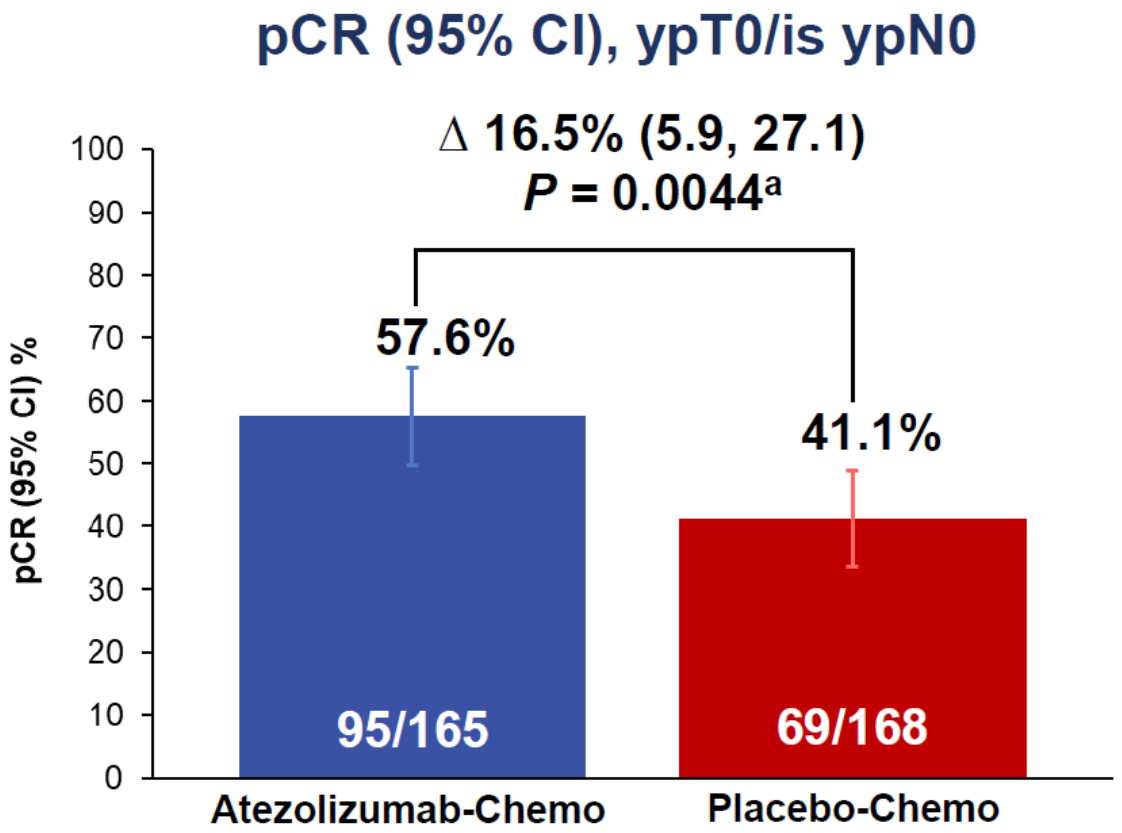
P Schmid et al *N Engl J Med* 2020;382:810-21.

Impassion 031



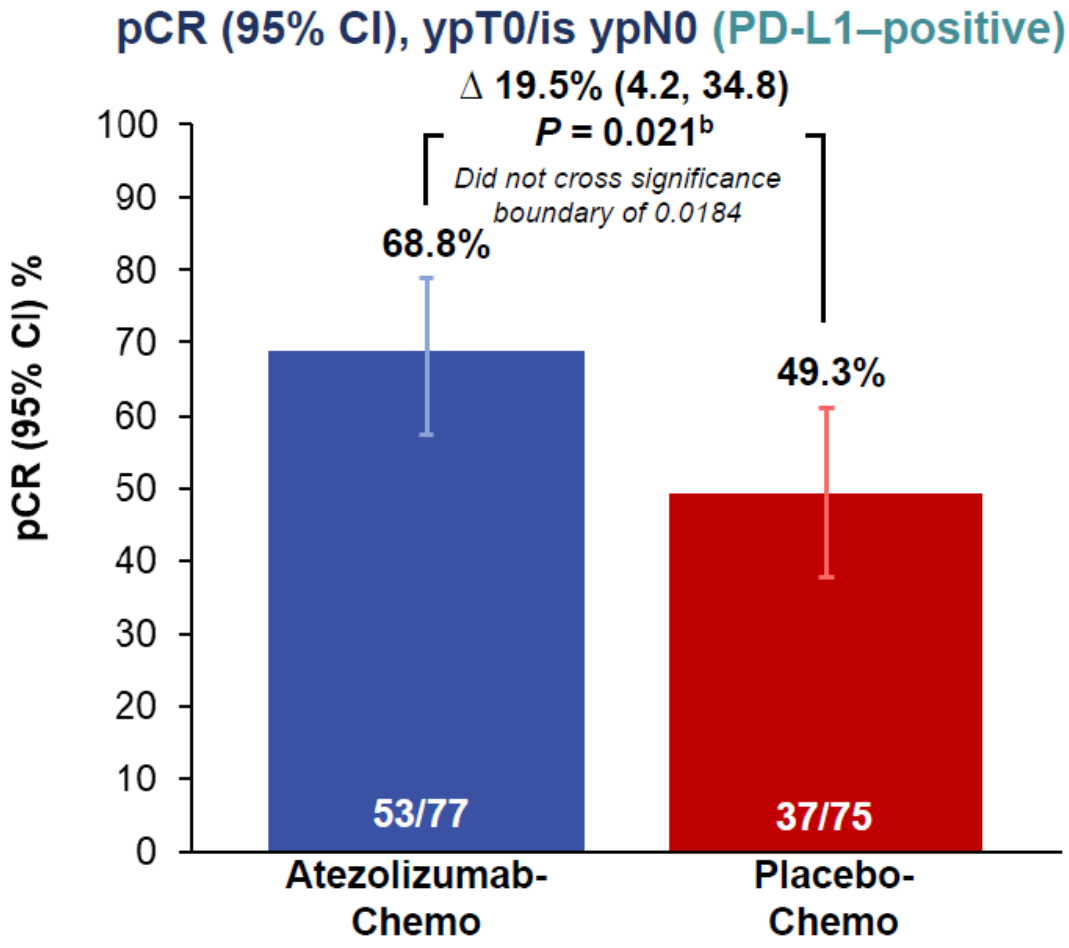
Mittendorf EA et al. *Lancet*. 2020 Oct 10;396(10257):1090-1100.

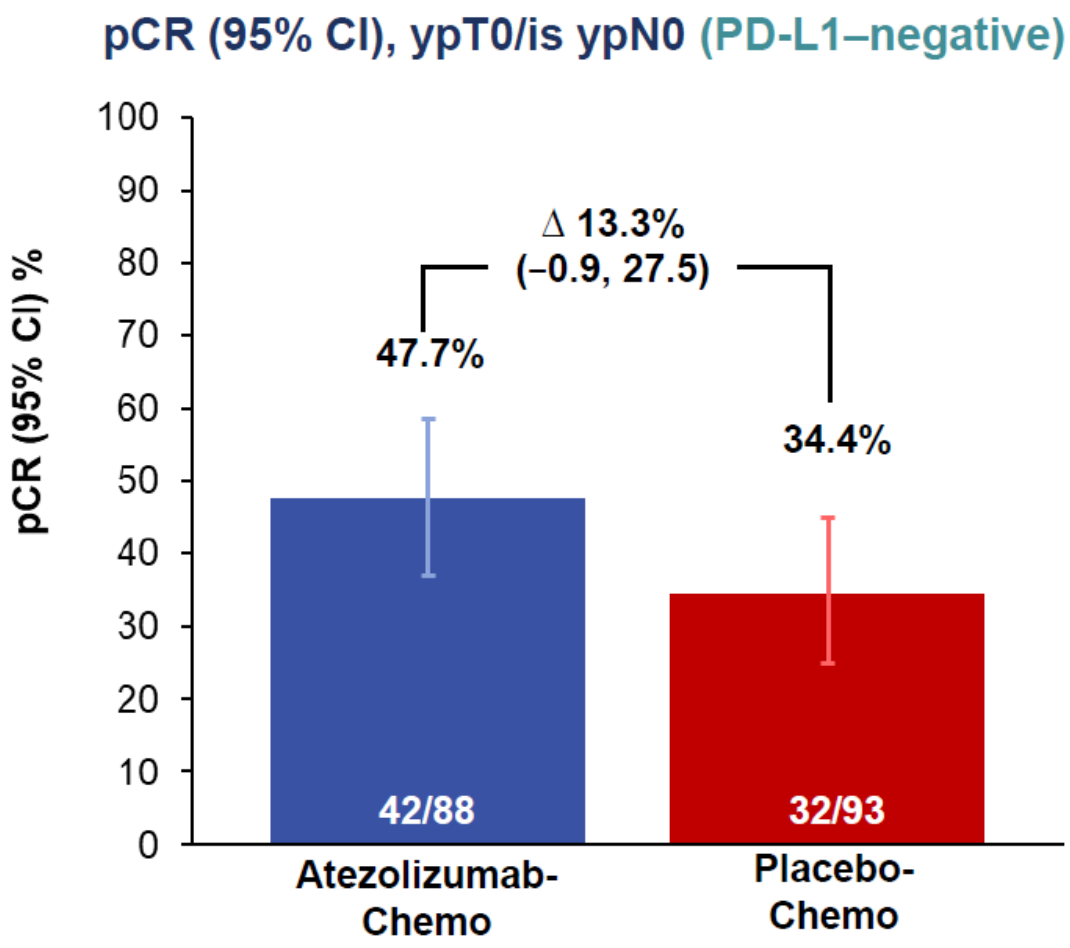
Impassion031: Co-primary endpoint pCR ITT



Mittendorf EA et al. *Lancet*. 2020 Oct 10;396(10257):1090-1100.

Impassion031: Co-primary endpoint pCR in PDL1+ tumors





Mittendorf EA et al. *Lancet*. 2020 Oct 10;396(10257):1090-1100.

Phase 3 IO + chemo neoadjuvant TNBC trials

Trial	Target	Chemotherapy	N	Open (Estimated Completion)	Primary endpoint(s)	Secondary endpoints	Eligibility	LN positive
IMpassion031 (NCT03197935)	PD-L1	Nab-paclitaxel, ddAC	333	July 2017 (Sept 2021)	**pCR ITT 58 vs 41%** pCR PD-L1+ 69 vs 49%$^{n.s.*}$	EFS, DFS, OS (all +trend), safety, PRO	T1N1-3 T2-4N0-3	36%
KEYNOTE-522 (NCT03036488)	PD-1	Paclitaxel + carbo, AC/EC	1150 (602)	March 2017 (March 2025)	**pCR ITT 65 vs 51%** EFS ITT (+ trend)	pCR PD-L1+ 69 vs 55%, EFS PD-L1+, OS	T1cN1-2 T2-4N0-2	51%
NeoTRIPaPDL1 (NCT02620280)	PD-L1	Nab-paclitaxel + carbo, postop AC/EC/FEC	280	April 2016 (October 2022)	5 yr-EFS (pending)	pCR ITT 44 vs 41%$^{n.s.}$, safety	T1cN1 T2N1 T3-4N0-3	87%
NSABP B-59 (NCT03281954)	PD-L1	Paclitaxel+ Carboplatin, AC/EC	1520	December 2017 (June 2024)	pCR (pending) EFS (pending)	OS, RFI, dDFS (all pending)	T1cN1-3 T2-3N0-3	n/a

IMpassion031: Atezolizumab 840/PLA q2w + nab-paclitaxel 125 q1w x 12 – Atezolizumab/PLA q2w + ddAC x 4 - surgery – atezolizumab 1200/PLA q3w to 1 year. Stratification stage II/III, PD-L1+/-.
KEYNOTE-522: Pembrolizumab 200/PLA q3w + weekly paclitaxel 80 + carboAUC1.5 qw or AUC 5 q3w x 4 cycles – pembrolizumab 200/PLA q3w + AC q3w x 4 - surgery – pembrolizumab 200/PLA q3w x 9 cycles. Stratification LN+/-, T1-2/3-4, Carbo qw/q3w.
NeoTRIP: open label Atezolizumab 1200/PLA q3w + Carboplatin AUC2 D1, 8 of 21 days + Nab-paclitaxel 125 D1, 8 of 21 days x 8 – surgery - AC/EC/FEC q3w (without adjuvant Atezolizumab/PLA). Stratification n/a.
NSABP B-59/GeparDouze: Weekly Paclitaxel 80 x 12 + Carboplatin AUC 5 q3w x 4 + Atezolizumab 1200 q3w x 4 - AC (or EC) q2-3w x 4 - surgery – Atezolizumab 1200 q3w until 1 year

* By hierarchical testing

Schmid et al, NEJM 2020, Mittendorf et al, Lancet 2020, Gianni et al SABCS 2019, Mittendorf et al, SABCS 2020

PD-L1 as biomarker (in neoadj setting)

- ✓PD-L1 positivity predicts higher likelihood of pCR but not who benefits from added IO

	IMpassion031	KEYNOTE-522	NeoTRIP
Assay (cutoff)	SP142 (IC 1%)	22C3 (CPS 1%)	SP142 (IC 1%)
PD-L1+ prevalence	46%	83%	54%
pCR (%): PD-L1+ | ITT | PD-L1-	**69 | 58 | 48**	**69 | 65 | 45**	**52 | 43 | 31**
pCR Δ: PD-L1+ | ITT | PD-L1-	**20 | 17 | 13**	**14 | 14 | 15**	**4 | 3 | 0**

- ✓Association of PD-L1 positivity with survival in neoadjuvant IO trials not yet known

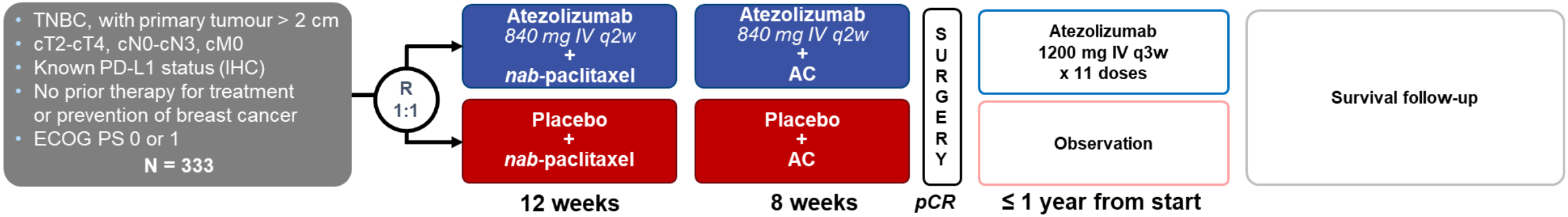
Safety of IO in early TNBC

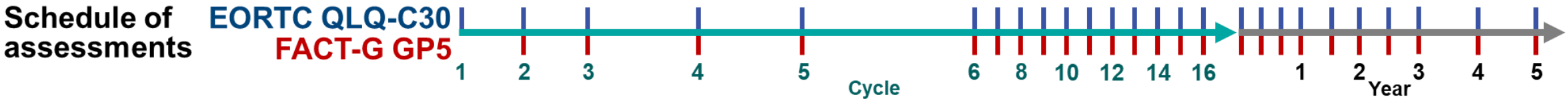
- Commonly reported AEs are similar between arms and mostly driven by chemotherapy
- Increased toxicity (Δ to chemotherapy arm)
  - Treatment-related G3/4 AE (3% in IMpassion031, 4% in KN-522, 7% in NeoTRIP)
  - Treatment-related G5 AE (0 in IMpassion031, 0.4% in KN-522, 0.7% in NeoTRIP)
  - IrAEs (10% in IMpassion031, 20% in KN-522)

- Practitioners need to be aware of common as well as rare but serious irAEs (such as adrenal insufficiency). Patient education and early intervention is key.
- Patients should be informed that endocrinopathies can result in life-long requirement for monitoring and supplementation.

PROs and immunotherapy

PRO (patient-reported outcomes): IMpassion031





Co-Primary endpoints:
- Pathologic complete response (ypT0/is ypN0) in ITT and PD-L1–positive[a] (IC≥1%) subpopulation

Secondary PRO endpoints:
- Mean and mean changes from baseline in function (role, physical) and global health status/HRQoL

Exploratory PRO endpoints:
- Mean and mean changes from baseline in function (emotional, social, cognitive), and disease and/or treatment-related symptoms
- Proportion of patients reporting each response option at each assessment time-point by treatment arm for the treatment bother item

Mittendorf E et al, SABCS 2020

PRO in breast cancer IO trials

Symptom Bother
(FACT-G Single Item, GP5)

Functional Assessment of Cancer Therapy-General **(FACT-G5)** "I am bothered by side-effects of treatment"

IMpassion031
Mittendorf E et al, SABCS 2020

EORTC Quality of Life — **EORTC QLQ-C30**

30 items assess the following domains during the past week

Domains	Patient functioning • Physical • Role • Social • Emotional • Cognitive	Symptom scales • Fatigue • Pain • Nausea/vomiting • Dyspnea	• Insomnia • Appetite loss • Constipation • Diarrhea	Financial difficulties	GHS/HRQoL
Scoring	1 – not at all to 4 – very much				1 – very poor to 7 – excellent

EORTC QLQ-BR23

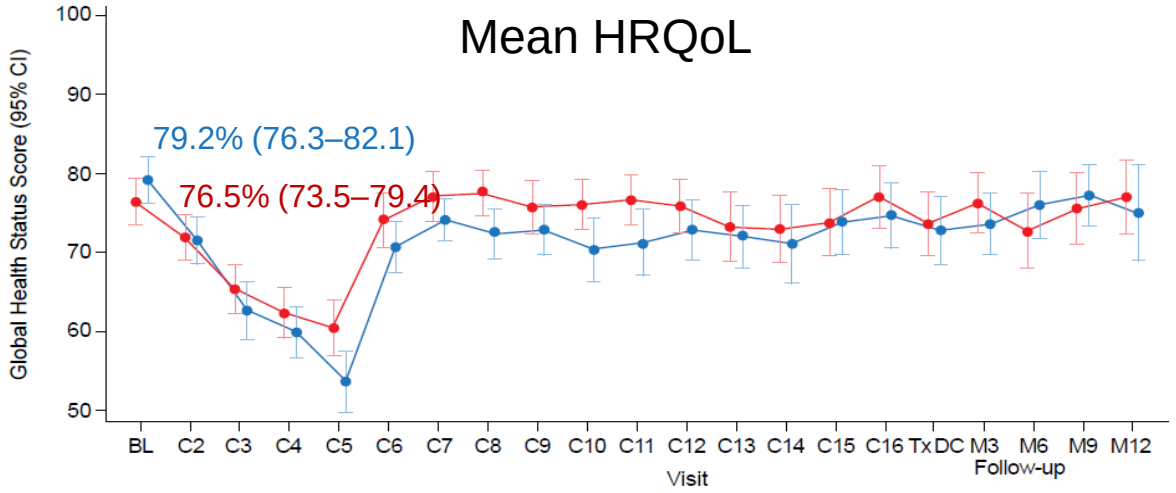
IMpassion130
Adams S et al, Ann Oncol. 2020

PRO in IMpassion 031

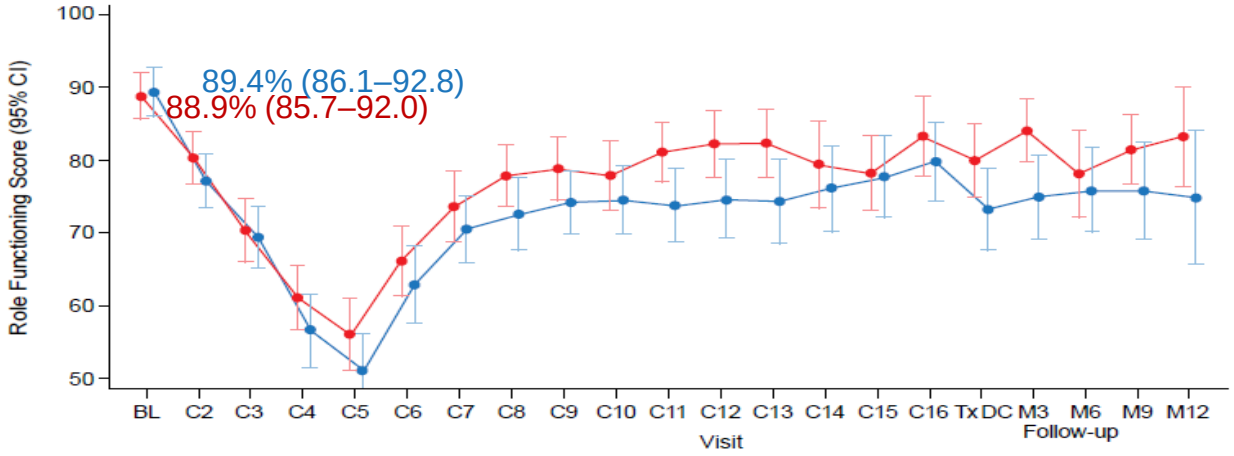
Atezolizumab + chemotherapy
Placebo + chemotherapy

Completion rates:
100% at baseline
90% at discontinuation

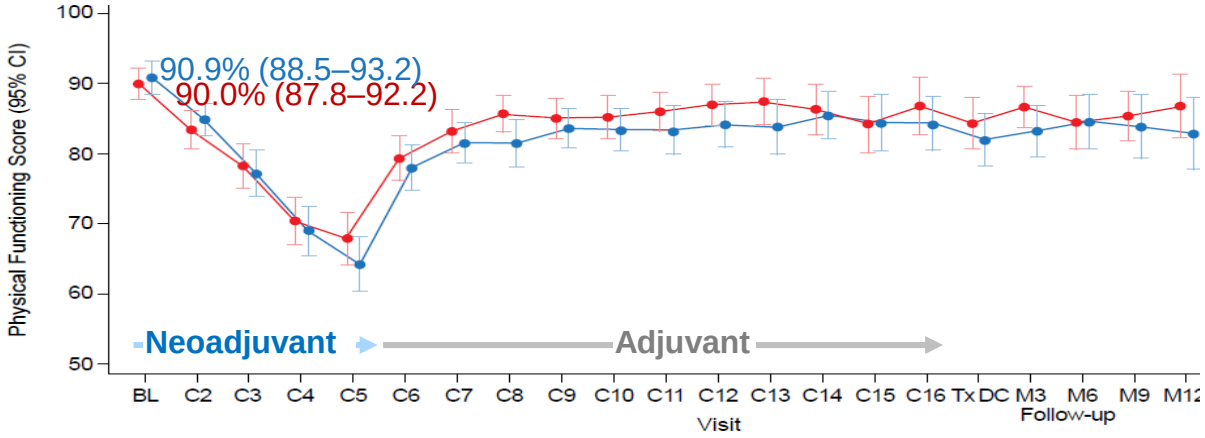
Mean HRQoL



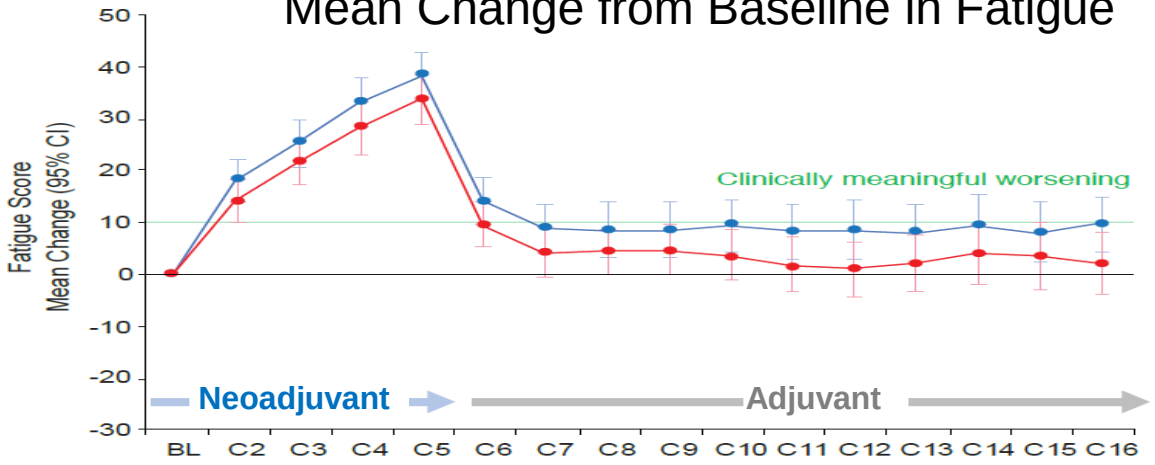
Mean Role Function



Mean Physical Function



Mean Change from Baseline in Fatigue

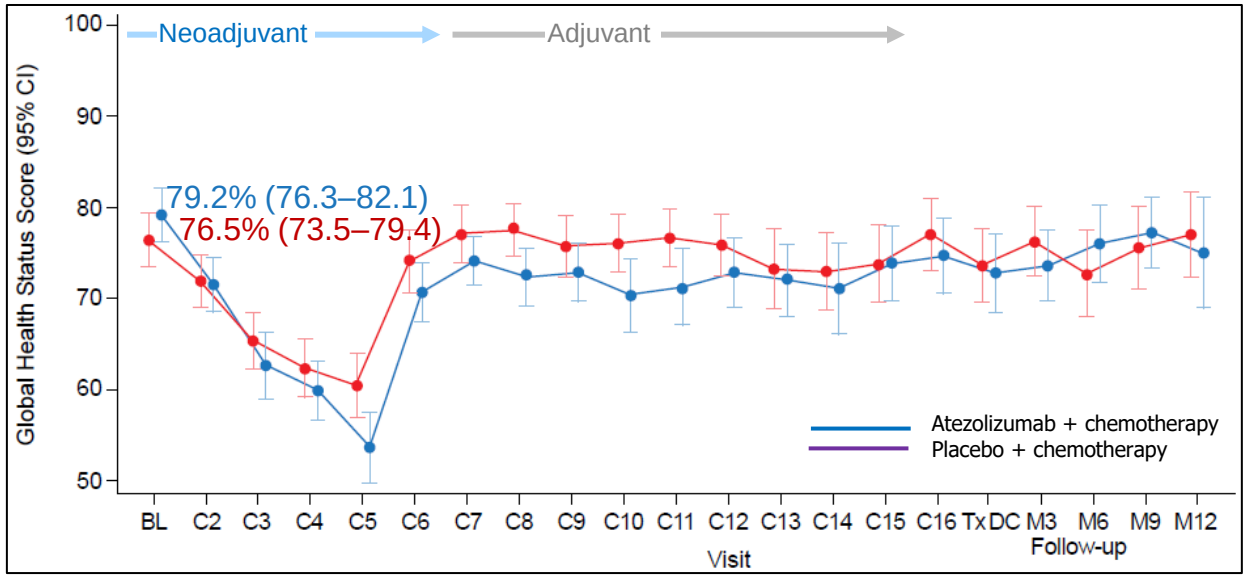


Mittendorf E et al, SABCS 2020

PRO in IO trials for early vs metastatic TNBC

Health-related QoL

IMpassion031

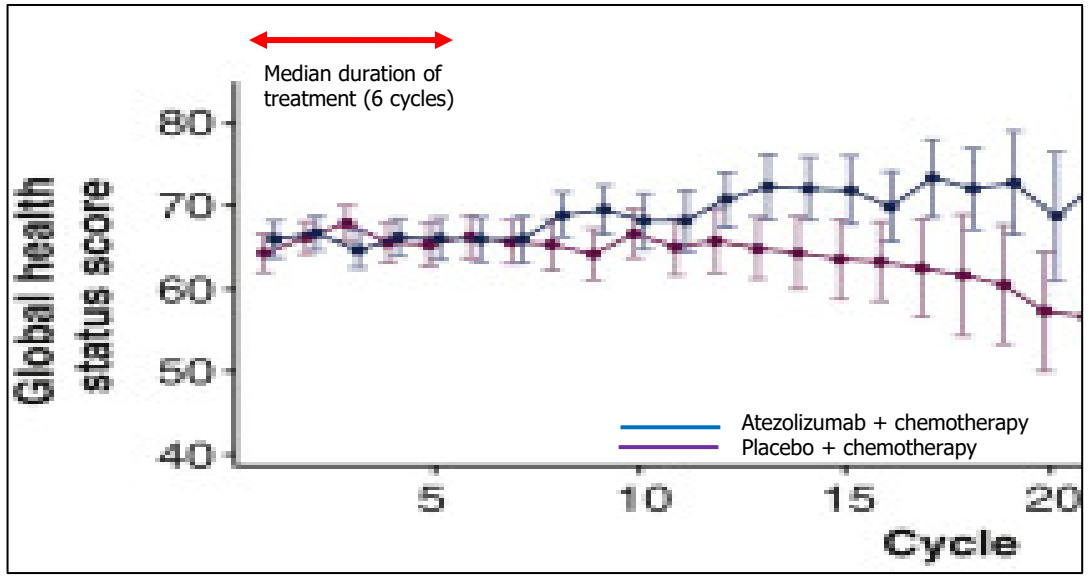


Baseline HRQoL (78), and functioning (90 physical, 89 role).

Neoadjuvant treatment - significant deterioration in HRQoL and functioning. Effects were transient, most pronounced during AC portion.

No additive burden with atezolizumab

IMpassion130



Baseline lower HRQoL (65), and functioning (80 physical, 73 role).

During study treatment – no significant deterioration in HRQoL and functioning.

No additive burden with atezolizumab

Mittendorf E et al, SABCS 2020, Adams S et al, Ann Oncol 2020

Summary IO in early TNBC

- Combining immune checkpoint inhibitors with neoadjuvant chemotherapy has been demonstrated in two RPh3 trials to improve pCR rates.
- Preliminary analyses of EFS appear promising.
- Toxicity is manageable.
- PRO for IMpassion031 reassuring that addition of atezolizumab did not impact HRQoL, but also shows that chemotherapy has a major impact on patients' well-being.

<u>Unmet needs & unanswered questions</u>

- De-escalation: Does every patient need chemotherapy? and immunotherapy?
- Lack of predictive biomarkers
- Does increased pCR after neoadjuvant IO + chemotherapy lead to improved survival?
- Optimization of chemotherapy backbone: Carboplatin? Anthracyclines? Sequencing?
- Results of adjuvant IO trials
    - A-Brave (NCT02926196, estimated completion date June 2023)
    - IMpassion030 (NCT03498716, estimated completion date December 2024)
    - SWOG S1418/BR006 (NCT02954874, estimated completion date May 2026)

Conclusions and Future Directions

- Addition of anti- PD-1/PD-L1 to chemotherapy is effective in TNBC
- Cure is a possibility with IO even in advanced TNBC

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- **Novel agents and combinations to improve outcomes**
- **Optimize chemo backbones**

- IO addition is relatively well tolerated, but chemotherapy is toxic and advanced cancer affects QoL

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- **Chemo de-escalation in setting of IO**
- **Prevention of recurrence**

- PD-L1 is not an ideal biomarker and prediction of benefit varies by disease setting

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- **Predictive biomarker research**


Seidman Cancer Center