Annual update on breast cancer 2019
From Trial to Clinical Practice

Triple Negative Breast Cancer

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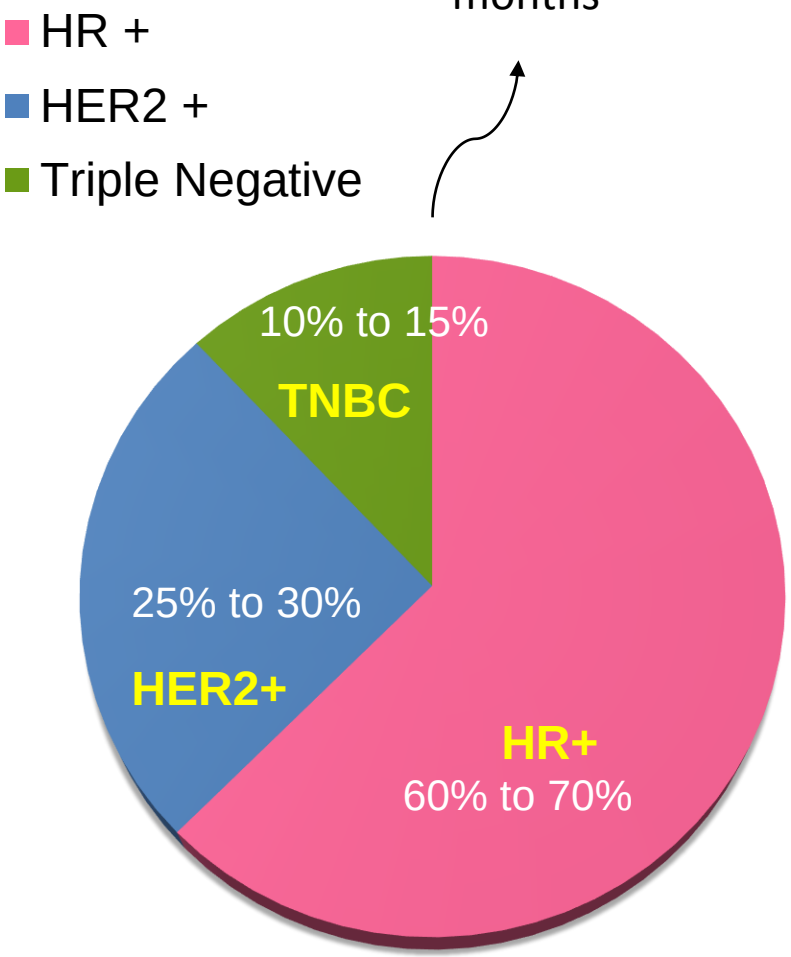
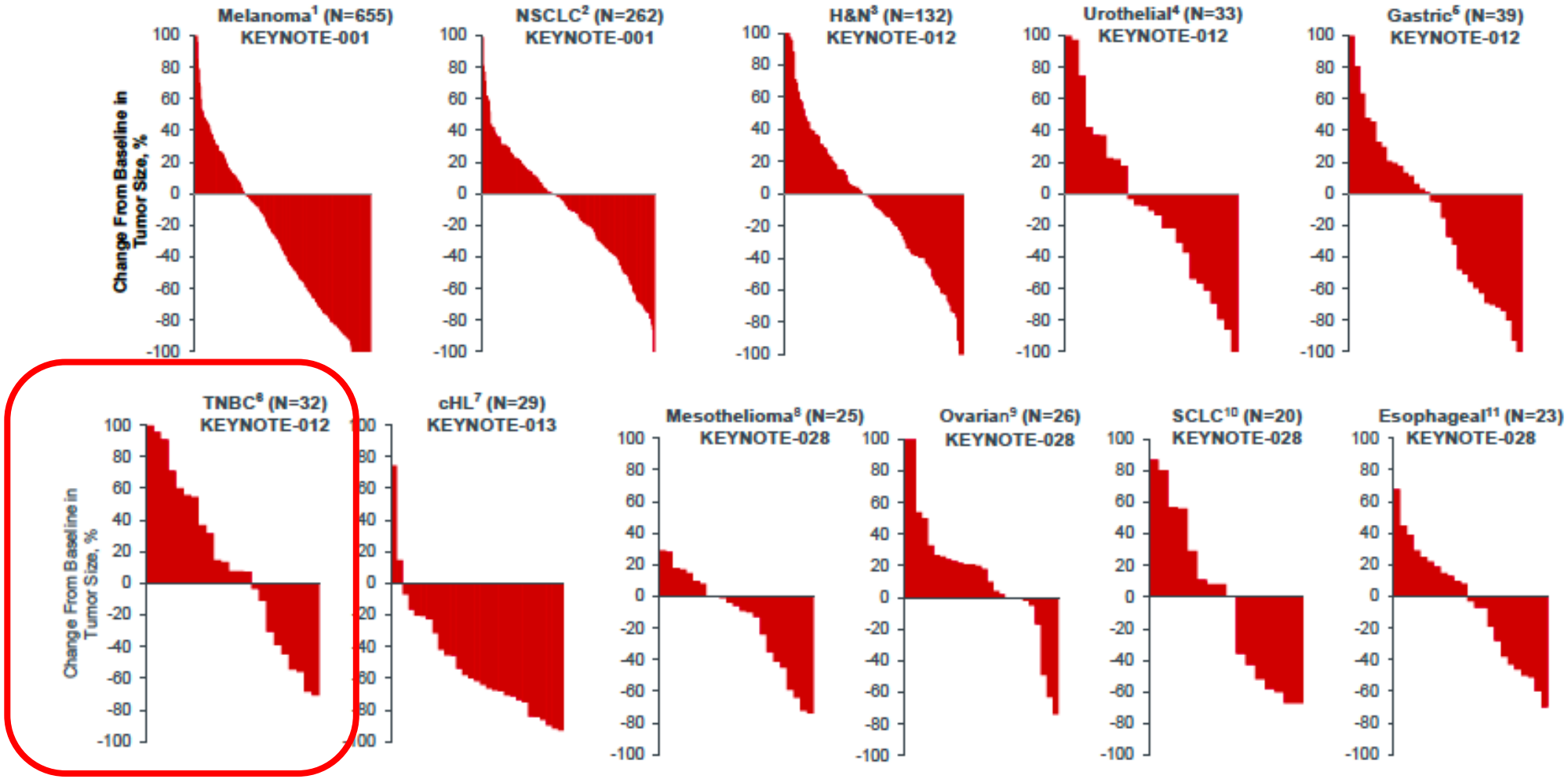
TNBC is a very aggressive breast cancer with median OS of 9-12 months



Systemic therapy for TNBC

- Chemotherapy
  - Anthracycline/cyclophosphamide
  - Taxane
  - Platinum
  - Eribulin…..
- Targeted therapy
  - Bevacizumab (FDA approval taken off in year 2011)
  - PARP inhibitor for gBRCA mutation (Olaparib, 2018; talazoparib, 2018)

Immunotherapy anti-PD1 pembrolizumab demonstrates broad anti-tumor activity



KEYNOTE-086: Phase 2 Study of Pembrolizumab in Metastatic TNBC

Cohort A:
Previously Treated
PD-L1 Unselected

386 patients screened

170 patients enrolled/treated
- **105 PD-L1 positive (61.8%)**
- **64 PD-L1 negative (37.6%)**
- **1 PD-L1 unknown (0.6%)**

	Previously Treated Any PD-L1 Expression Cohort A			*First Line PD-L1 Selected*
	All (n=170)	**PD-L1+ (n=105)**	**PD-L1- (n=64)**	***PD-L1+ (n=52)***
ORR, %	4.7%	4.8%	4.7%	*23.1%*
DCR, %	7.6%	9.5%	4.6%	
CR, n	1	1	0	
PR, n	7	4	3	
SD, n	35	22	112	

PD-L1 is an imperfect biomarker; context is important.

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Chen & Han, J Clin Invest 2015; 125(9):3384-3391

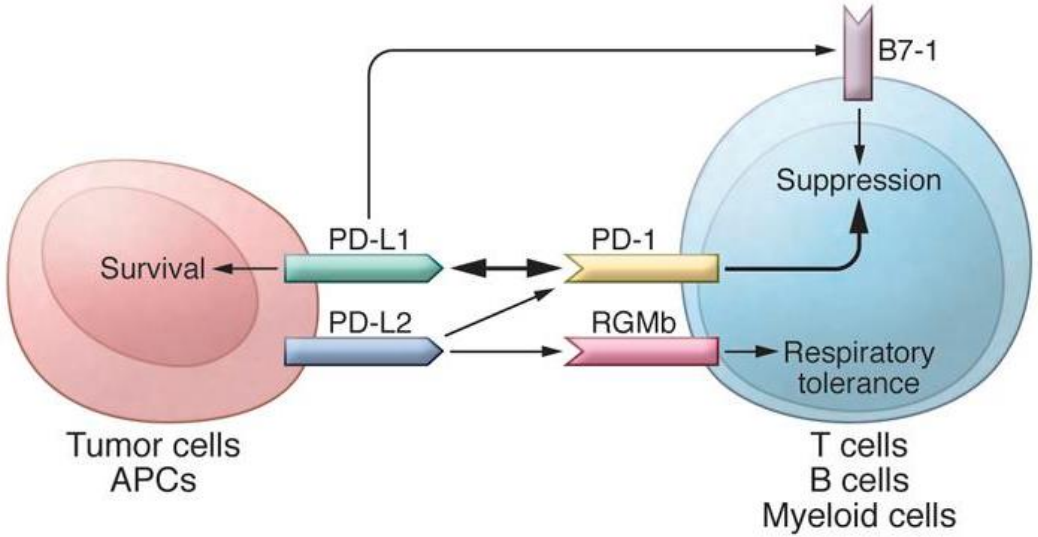


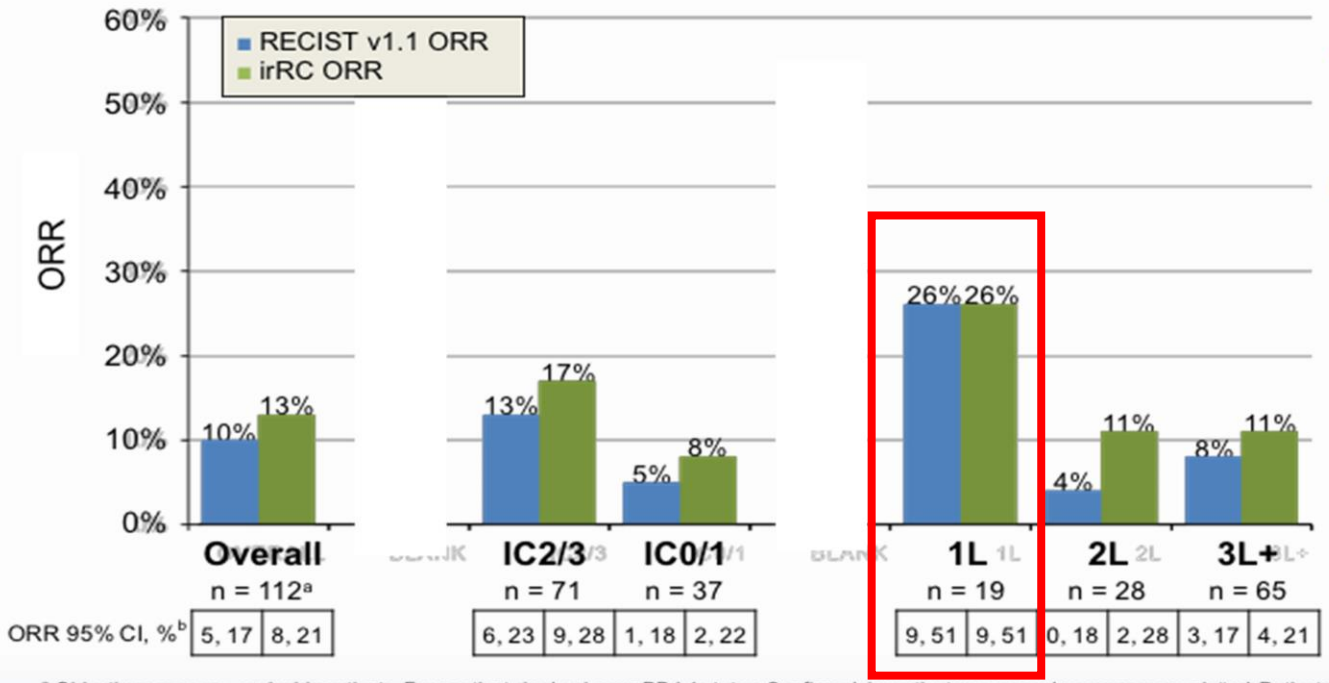
Figure 1

The PD pathway.

The PD pathway has at least 5 interacting molecules. PD-L1 and PD-L2, with different expression patterns, were identified as ligands of PD-1, and the interaction of PD-L1 or PD-L2 with PD-1 may induce T cell suppression. PD-L1 was found to interact with B7-1 (CD80) on activated T cells and inhibit T cell activity. PD-L2 has a second receptor, RGMb; initially, this interaction activates T cells, but it subsequently induces respiratory tolerance. PD-L1 on tumor cells can also act as a receptor, and the signal delivered from PD-1 on T cells can protect tumor cells from cytotoxic lysis.

Company	Anti-PD1	Anti-PDL1
BMS	Nivolumab	
Merck	Pembrolizumab	
Pfizer		Avelumab
Roche/Genetech		**Atezolizumab** (MPDL3280A)
Novartis	PDR001	?
MedImmune/AstraZeneca		Durvalumab (MEDI4736)
Regeneron/Sanofi	REGN2810	

Atezolizumab in Metastatic TNBC



- Numerically higher ORRs were observed in IC2/3 and 1L subgroups
- irRC criteria captured non-classical responses to atezolizumab

[a] Objective response–evaluable patients. Four patients had unknown PD-L1 status. Confirmed, investigator-assessed responses are plotted. Patients with missing or unevaluable responses are included (16 per RECIST v1.1 and 23 per irRC). [b] ORR 95% CI was estimated using Clopper-Pearson method. Data cutoff: March 31, 2016.

Schmid P, et al. AACR 2017
Phase Ia Atezolizumab in TNBC

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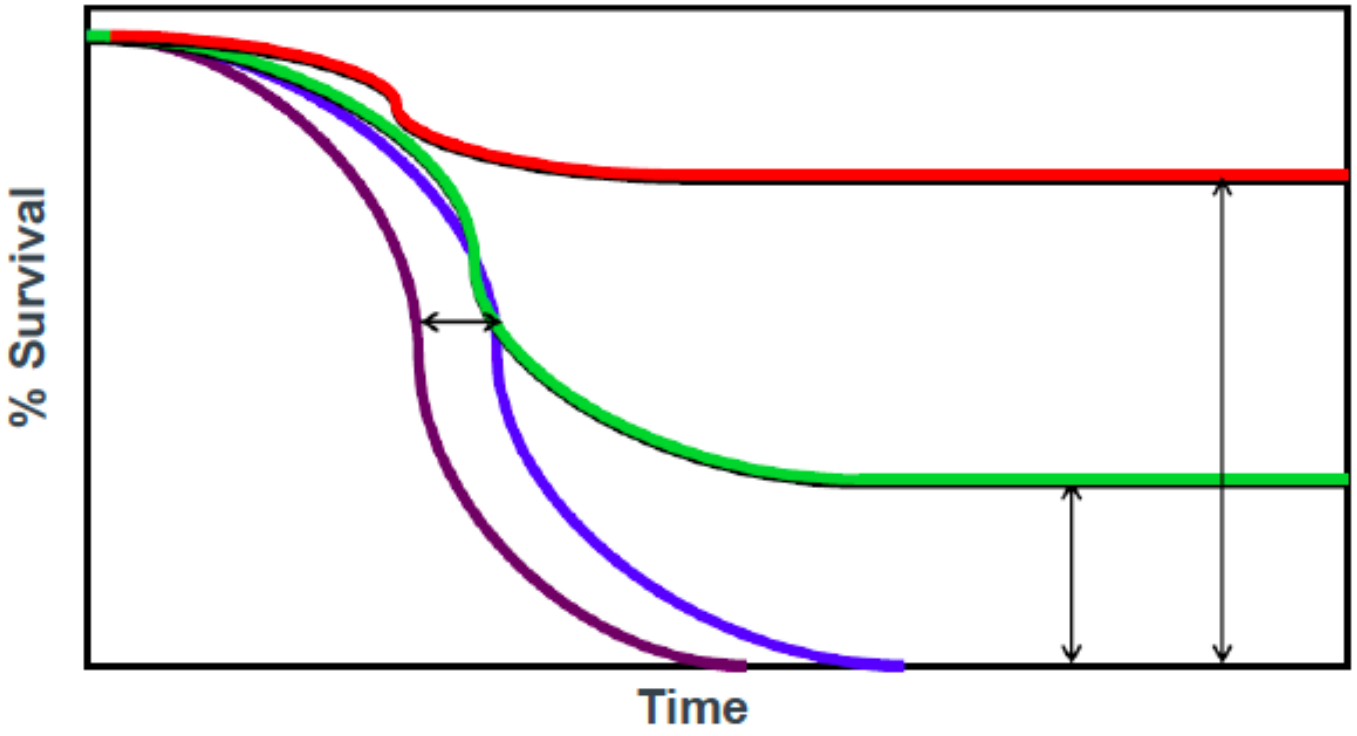
Augmenting effect of immunotherapy



Adding:

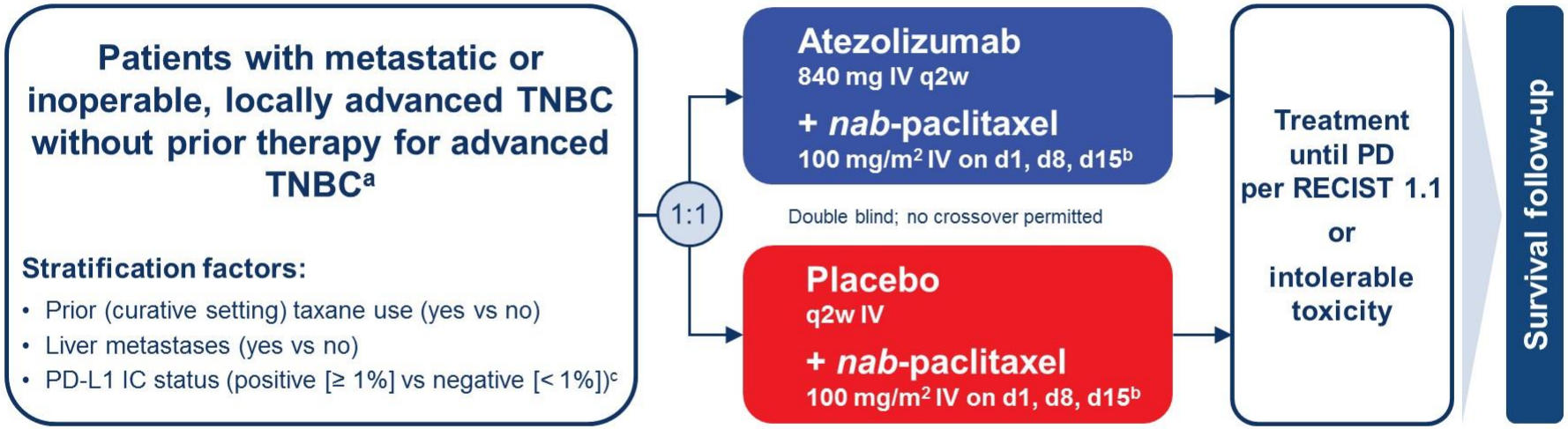
- Targeted agent?
- Radiotherapy?
- 2nd immunotherapy?
- Chemotherapy?

Can chemotherapy increase treatment response and survival?

No Treatment
Standard Treatment

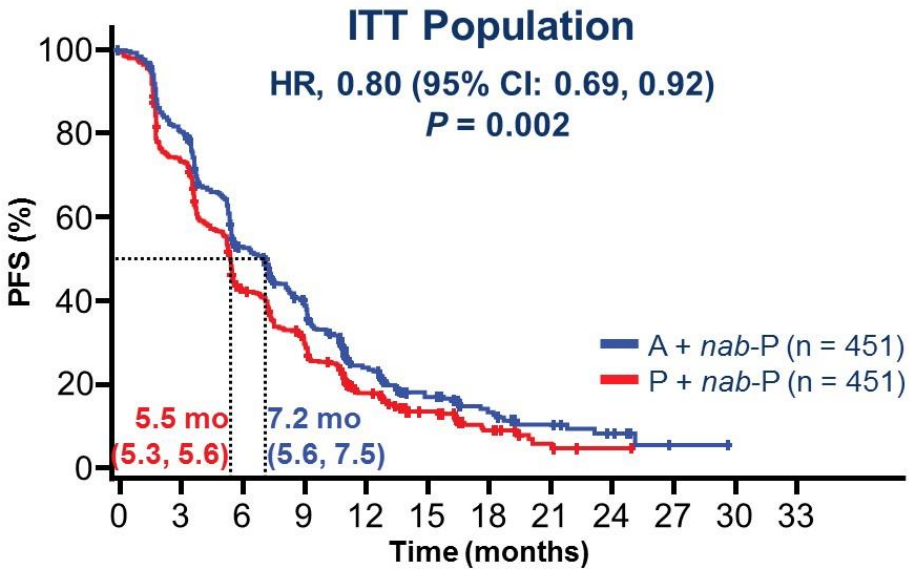
Checkpoint blockade
Combination Treatment

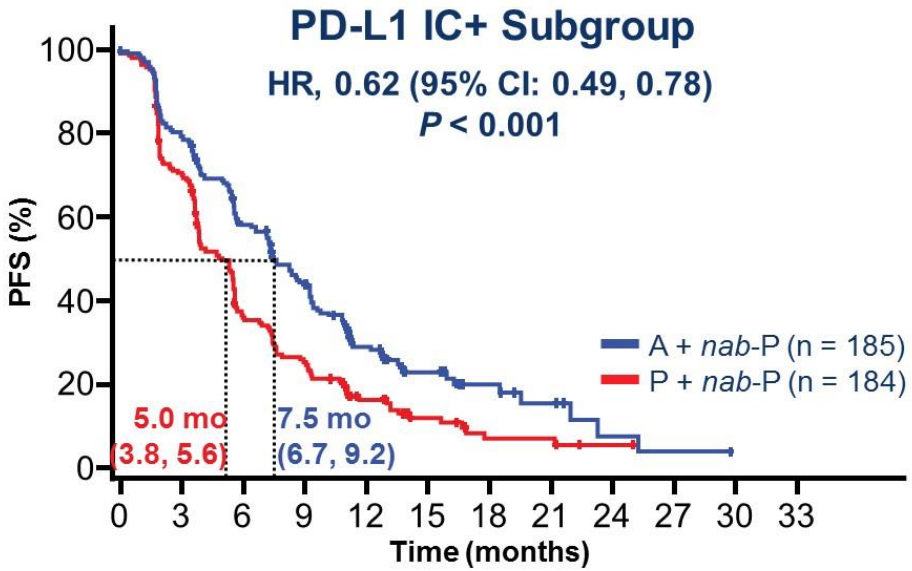
IMpassion130 Study Design



- 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+

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



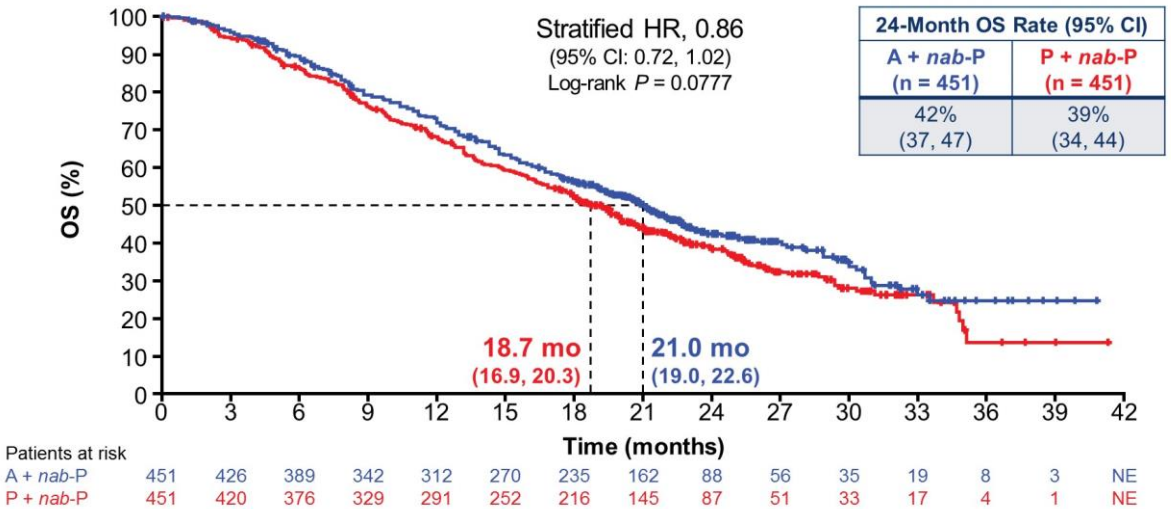


- PFS benefit driven by PD-L1 IC+ patients, as a treatment effect was not observed in PD-L1 IC− patients[1]

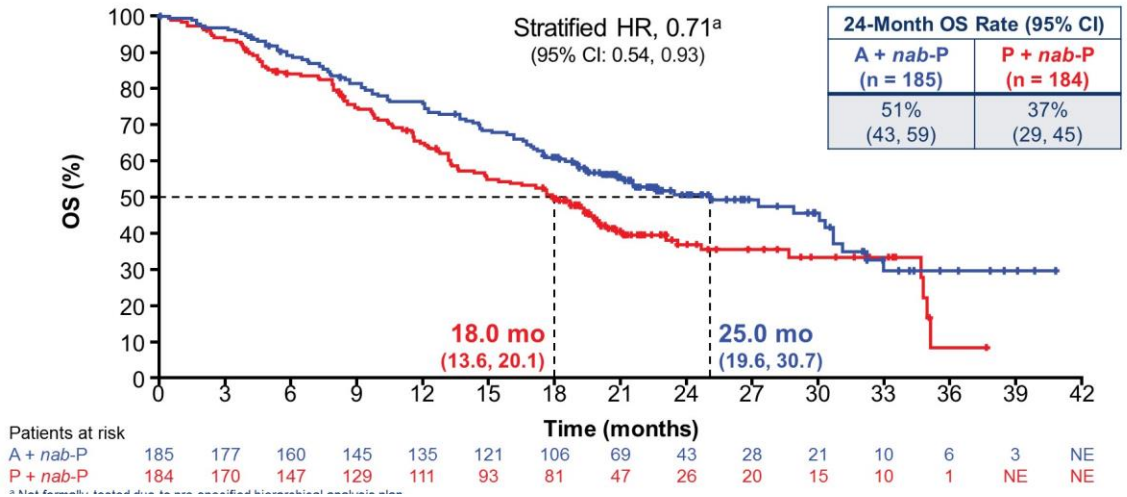
NCCN & AGO guidelines: Base on these data, atezolizumab + nab-paclitaxel received accelerated approval by the FDA in March 2019 and is recommended for patients with PD-L1 IC+ mTNBC

IMpassion130: updated OS from a global, randomized, double-blind, placebo-controlled, Phase III study of atezolizumab + *nab*-paclitaxel in previously untreated locally advanced or metastatic TNBC

OS in ITT Population



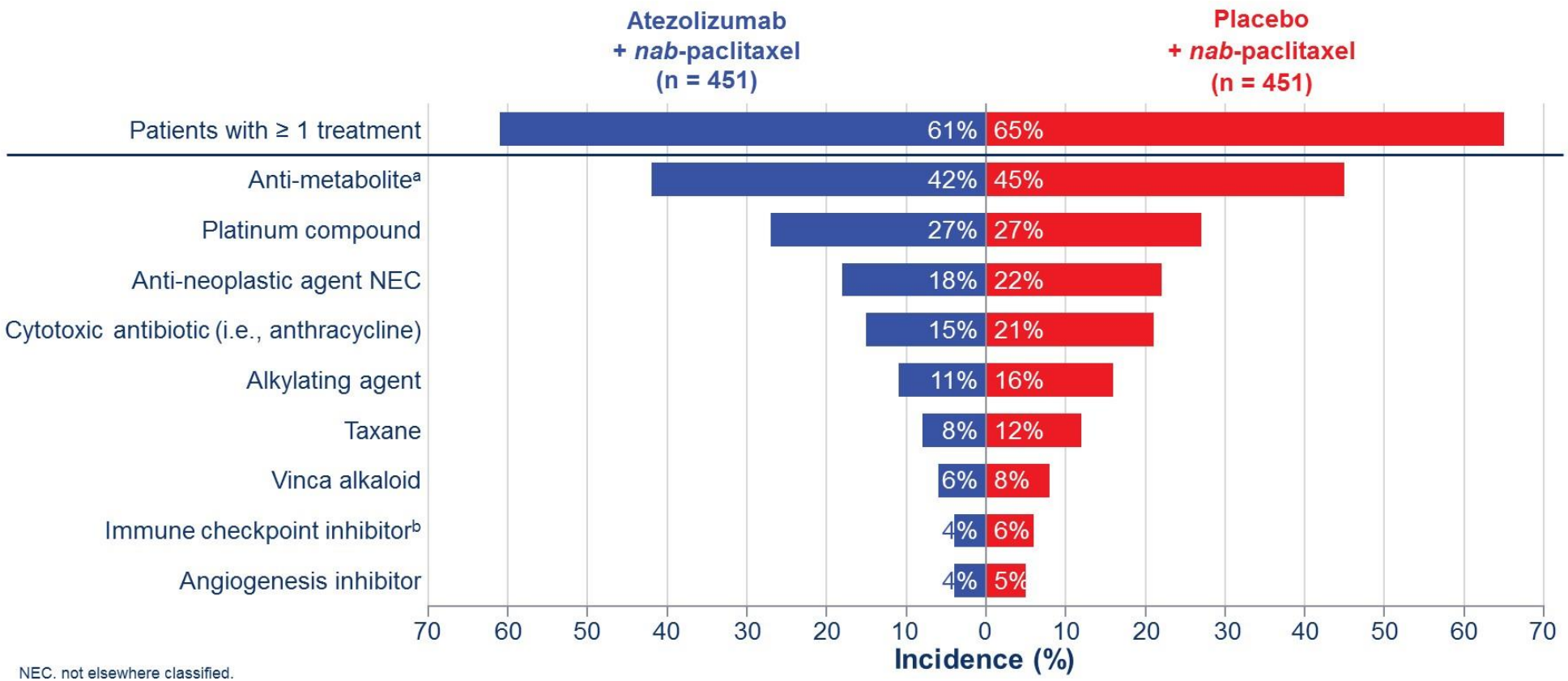
OS in PD-L1+ Population



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)

The objective response rate was higher with the combination compared to chemotherapy alone for all patients (56% vs 46%) and those with PD-L1–positive tumors (59% vs 43%).

Subsequent Therapies



NEC. not elsewhere classified.

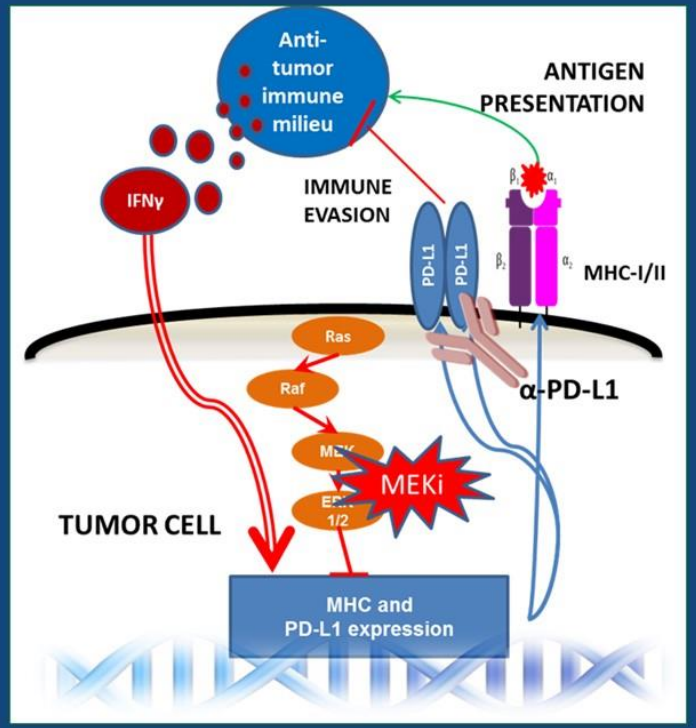
Conclusions

- IMpassion130 is the first and only Phase III study to show the clinically meaningful benefit of first-line immunotherapy in mTNBC
- PD-L1 IC status predicts clinical benefit with atezolizumab + *nab*-paclitaxel
- Although not formally testable due to the pre-specified statistical analysis plan, a median OS improvement from 18 to 25 months was observed in the PD-L1+ population (HR, 0.71)
- Atezolizumab + *nab*-paclitaxel was well tolerated, with no cumulative toxicities and no new- or late-onset safety signals
- Atezolizumab + *nab*-paclitaxel sets a new benchmark as the first therapy to cross the 2-year landmark OS benefit in first-line therapy for PD-L1+ mTNBC
- Atezolizumab + *nab*-paclitaxel is approved by the FDA[1] and recommended for the treatment of patients with PD-L1 IC+ mTNBC in the NCCN[2] and AGO[3] guidelines

Are there any strategy to boost treatment response further?

Can targeted agents improve response?

- The MEK pathway is active in TNBC
- Activation suppresses inflammatory responses to T cells, leading to reduced antigen presentation and PD-L1 expression
- Combining MEK inhibitors with anti-PD-L1 inhibitors may improve antigen presentation while blocking PD-L1-mediated suppression



Phase II COLET Study: Atezolizumab + Cobimetinib + Paclitaxel/*nab*-Paclitaxel as First-Line Treatment for Patients With Locally Advanced or Metastatic Triple-Negative Breast Cancer

Abstract #1013
Poster #94

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BACKGROUND

- Triple-negative breast cancer (TNBC) is characterized by the lack of estrogen and progesterone receptor (ER, PR) expression and the lack of overexpression or gene amplification of human epidermal growth factor 2 receptor (HER2)[1]
- Unlike for ER/PR-positive and HER2-positive breast cancers, chemotherapy has been the standard of care for first-line treatment of TNBC[2,3]
  - However, responses to chemotherapy are typically not durable, and the prognosis for patients with metastatic TNBC remains poor[4-8]
- Studies have indicated that the use of mitogen-activated protein kinase/extracellular signal-regulated kinase (MEK) inhibitor may help to overcome taxane resistance[9,10]
  - The Phase II COLET study (NCT02322814) previously showed that the addition of cobimetinib to paclitaxel resulted in an increased overall response rate (ORR) of 38% compared with 21% with placebo + paclitaxel in patients with locally advanced or metastatic TNBC.[11]
- The use of atezolizumab + *nab*-paclitaxel in the pivotal Phase III IMpassion130 study (NCT02425891) has also shown promising results in the first-line treatment of patients with advanced or metastatic TNBC, leading to accelerated US Food and Drug Administration approval for those whose tumors express programmed death-ligand 1 (PD-L1)[12]
- We present data from cohorts II and III from the COLET study, which investigated the efficacy and safety of atezolizumab + cobimetinib + paclitaxel and atezolizumab + cobimetinib + *nab*-paclitaxel, respectively, in patients with locally advanced or metastatic TNBC

OBJECTIVE

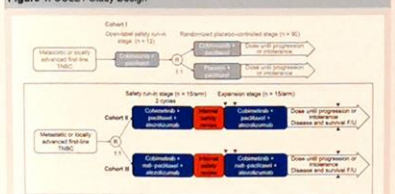
- To estimate the clinical benefit with atezolizumab + cobimetinib + paclitaxel or *nab*-paclitaxel, as measured by ORR

METHODS

Study Design

- COLET is a multi-stage, multi-cohort, Phase II, multi-center trial (Figure 1)

Figure 1. COLET Study Design



Patients and Treatments

- Eligible patients were female, aged ≥ 18 years with previously untreated, histologically confirmed locally advanced or metastatic TNBC and had an Eastern Cooperative Oncology Group performance status (ECOG PS) of 0 or 1 and no untreated or progressive central nervous system metastases
- Patients with left ventricular ejection fraction below the institutional lower limit of normal or < 50%, whichever was lower, or Grade ≥ 2 peripheral neuropathy, were excluded
- Patients were randomized 1:1 to receive first-line treatment with either atezolizumab 840 mg intravenously (IV) on days 1 and 15 + cobimetinib 60 mg once daily on days 3-23 + paclitaxel 80 mg/m^2 IV on days 1, 8 and 15 (Cohort II) or atezolizumab + cobimetinib + *nab*-paclitaxel 100 mg/m^2, IV on days 1, 8 and 15 (Cohort III) in 28-day cycles until disease progression or unacceptable toxicity
  - The intention-to-treat (ITT) population was defined as all randomized patients
  - The safety-evaluable population was defined as patients who received any amount of any study drug
- Dose modifications, interruptions and delays of study treatment were permitted in cases of adverse events (AEs) according to guidelines specified in the protocol.

Endpoints

- The primary endpoint was investigator-assessed confirmed ORR per Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST 1.1)
- Secondary endpoints included
  - Duration of response (DOR)
  - Investigator-assessed progression-free survival (PFS) per RECIST 1.1
  - Investigator-assessed unconfirmed ORR per RECIST 1.1
  - Overall survival (OS)
  - Safety
- Exploratory endpoints included
  - Efficacy by PD-L1 status

RESULTS

Patients

- Between November 2016 and April 2018, 63 patients were enrolled into Cohorts II and III. All data presented are per a data cutoff date of August 10, 2018
- 32 and 31 patients were randomized to Cohorts II and III, respectively
- Median duration of follow-up was 6.5 months
- Baseline demographics were generally well balanced and are summarized in Table 1

Table 1. Patient Baseline Demographics

	Atezo + Cobi + Pac (n = 32)	Atezo + Cobi + *nab*-Pac (n = 31)
Median age (range), years	52 (26-79)	51 (20-75)
< 65 years, n (%)	24 (75)	26 (84)
≥ 65 years, n (%)	8 (25)	5 (16)
Race, n (%)		
Asian	2 (6)	5 (16)
Black or African American	1 (3)	0
White	28 (88)	25 (81)
Other	1 (3)	1 (3)
Prior neoadjuvant/adjuvant taxane therapy, n (%)		
No	11 (34)	11 (36)
Yes	21 (66)	20 (65)
Disease-free interval from last chemotherapy, n (%)		
≤ 12 months	9 (28)	6 (19)
> 12 months/no prior chemotherapy	23 (72)	25 (81)

Atezo, atezolizumab; Cobi, cobimetinib; Pac, paclitaxel.

Efficacy

- Investigator-assessed ORR and DOR are summarized in Table 2.

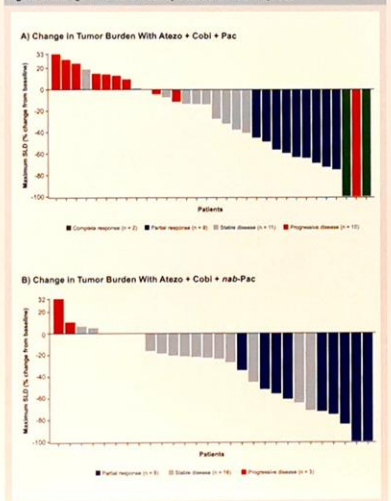
Table 2. Investigator-Assessed ORR and DOR

Best Overall Response	Atezo + Cobi + Pac (n = 32)	Atezo + Cobi + *nab*-Pac (n = 31)
Objective response rate (95% CI), n (%)	34.4 (18.6, 53.2)	29.0 (14.2, 48.0)
Complete response, %	2 (6)	0
Partial response, %	9 (28)	9 (29)
Stable disease, %	11 (34)	16 (52)
Progressive disease, %	10 (31)	3 (10)
Not done, %	0	3 (10)
Duration of Response	**(n = 11)**	**(n = 9)**
Median duration of response (95% CI), months	5.8 (4.4, NE)	11.0 (7.3, NE)
Range	1.9*-14.9*	1.8*-11.6*

NE, not estimable; *, censored.

- Change in tumor burden by best confirmed response is shown in Figure 2

Figure 2. Change in Tumor Burden by Best Confirmed Response



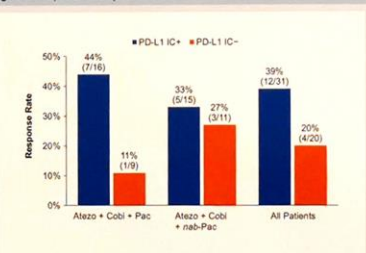
- Investigator-assessed PFS and OS are summarized in Table 3

Table 3. Investigator-Assessed PFS and OS

	Atezo + Cobi + Pac (n = 32)	Atezo + Cobi + *nab*-Pac (n = 31)
Median PFS (95% CI), months	3.8 (3.0, 7.4)	7.0 (3.7, 12.8)
Median OS (95% CI), months	11.0 (9.5, NE)	NE (10.2, NE)

- Response by PD-L1 status is shown in Figure 3. Response rates from cohort II and III were aggregated for exploratory purposes only and are not controlled for differences between the two treatment arms. Careful interpretation is advised

Figure 3. Response Rate by PD-L1 Status[a]



IC, tumor-infiltrating immune cells.
[a] PD-L1 IC+, ≥ 1% of tumor area containing PD-L1 stained IC; PD-L1 IC−, < 1% of tumor area containing PD-L1 stained IC.

- Median PFS and OS by PD-L1 status are shown in Table 4

Table 4. Median PFS and OS by PD-L1 Status[a]

	Atezo + cobi + Pac		Atezo + cobi + *nab*-Pac	
	PD-L1- n = 9	PD-L1+ n =16	PD-L1- n = 11	PD-L1+ n =15
Median PFS, mo (95% CI)	3.7 (1.9, 5.6)	9.0 (1.9, 9.0)	5.6 (2.1, NE)	7.0 (3.7, 9.1)
Median OS, months (95% CI)	11.0 (5.5, NE)	10.5 (9.5, NE)	NE (9.4, NE)	NE (10.2, NE)

[a] PD-L1 IC+, ≥ 1% of tumor area containing PD-L1 stained IC; PD-L1 IC−, < 1% of tumor area containing PD-L1 stained IC.

Safety

- The safety summary is shown in Table 5.
- Grade 3+ AEs occurred in 69% of patients in the atezolizumab + cobimetinib + paclitaxel cohort and 70% of patients in the atezolizumab + cobimetinib + *nab*-paclitaxel cohort
- Serious AEs occurred in 47% of patients in the atezolizumab + cobimetinib + paclitaxel cohort and 43% of patients in the atezolizumab + cobimetinib + *nab*-paclitaxel cohort
- AEs were generally tolerable and manageable in both cohorts
  - Discontinuation of atezolizumab due to AEs was low in both arms, occurring in 13% patients in the atezolizumab + cobimetinib + paclitaxel cohort and 3% of the patients in the atezolizumab + cobimetinib + *nab*-paclitaxel cohort
  - Discontinuation of cobimetinib due to AEs occurred in 13% patients in the atezolizumab + cobimetinib +paclitaxel cohort and 17% of the patients in the atezolizumab + cobimetinib + *nab*-paclitaxel cohort
- Two grade 5 AEs occurred in Cohort II. Grade 5 AEs included pulmonary embolism and lung infiltration. Both Grade 5 events were not suspected to be related to study treatment; the reported suspected causes were metastatic TNBC and disease progression, respectively.

Table 5. Safety Summary

n (%)	Atezo + Cobi + Pac (n = 32)	Atezo + Cobi + *nab*-Pac (n = 30)
Any AE	32 (100)	30 (100)
Grade 3-5	22 (69)	21 (70)
Grade 5	2 (6)	0
Serious AEs	15 (47)	13 (43)
AE leading to withdrawal of cobi	4 (13)	5 (17)
AE leading to withdrawal of atezo	4 (13)	1 (3)
No. of patients withdrawn from the study due to AE	0	0

- The incidence of AEs by preferred term is shown in Table 6
- Diarrhea was the most common AE, was more frequent with atezolizumab + cobimetinib + *nab*-paclitaxel than atezolizumab + cobimetinib + paclitaxel, and required intervention with anti-diarrheal treatment in both arms (74% and 56%, respectively)
- Gastrointestinal AEs of any grade were observed more frequently with atezolizumab + cobimetinib + *nab*-paclitaxel than with atezolizumab + cobimetinib + paclitaxel

Table 6. AEs Occurring in ≥ 20% of Patients

AE, n (%)	Atezo + Cobi + Pac (n = 32)		Atezo + Cobi + *nab*-Pac (n = 30)	
	All grades	≥ Grade 3	All grades	≥ Grade 3
Diarrhea	21 (66)	3 (9)	27 (90)	5 (17)
Nausea	13 (41)	1 (3)	15 (50)	0
Vomiting	9 (28)	1 (3)	12 (40)	1 (3)
Constipation	6 (19)	0	8 (27)	0
Rash	12 (38)	1 (3)	16 (53)	1 (3)
Anemia	14 (44)	4 (13)	10 (33)	3 (10)
Fatigue	11 (34)	1 (3)	10 (33)	2 (7)
Alopecia	8 (25)	0	10 (33)	0
Pyrexia	5 (16)	1 (3)	11 (37)	0
Dermatitis acneiform	8 (25)	2 (6)	6 (20)	1 (3)
Epistaxis	7 (22)	0	7 (23)	0
Neuropathy peripheral	7 (22)	1 (3)	6 (20)	2 (7)

CONCLUSIONS

- COLET is the first study to evaluate a PD-L1 inhibitor, a MEK inhibitor and a taxane combination (atezolizumab + cobimetinib + taxane), which showed activity as first-line treatment for locally advanced or metastatic TNBC
- The triplet combination of atezolizumab + cobimetinib + taxane showed a modest ORR in this locally advanced/metastatic TNBC population
- At a median follow up of 6.5 months, the number of DOR and PFS events were small, and firm conclusions cannot be drawn
- Patients with PDL1 IC+ tumors trended toward increased ORR but patient numbers are small and should be interpreted with caution
  - The ORR was 39% in PD-L1 IC+ patients and 20% in PD-L1 IC− patients
- The safety profile of atezolizumab + cobimetinib + paclitaxel/*nab*-paclitaxel was consistent with that reported for the individual drugs. No new or unexpected AEs were observed
  - Diarrhea was the most commonly reported AE, was mostly grade 1 and 2, and was more common in the *nab*-paclitaxel arm
- Study treatment regimens were tolerable with < 20% treatment discontinuations due to AEs

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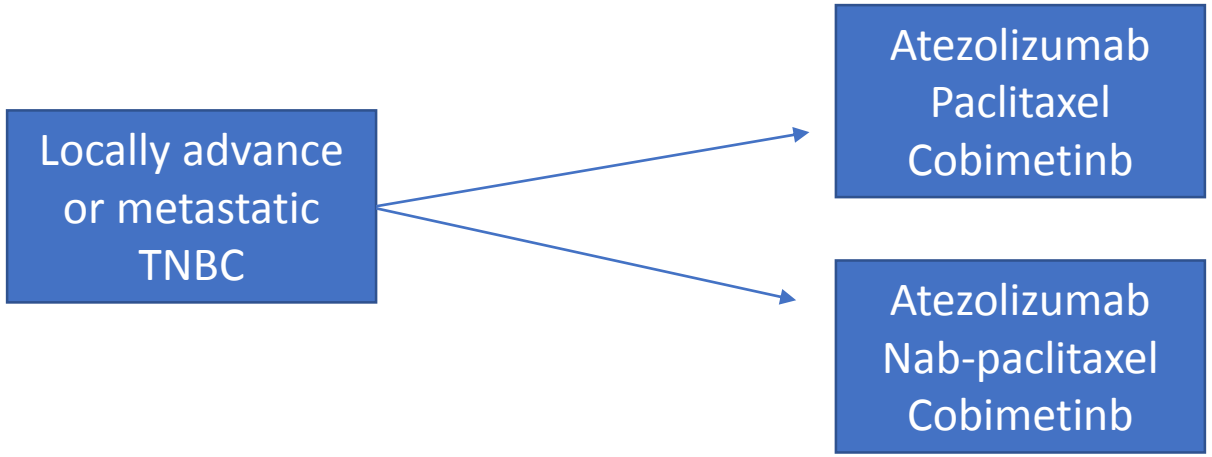
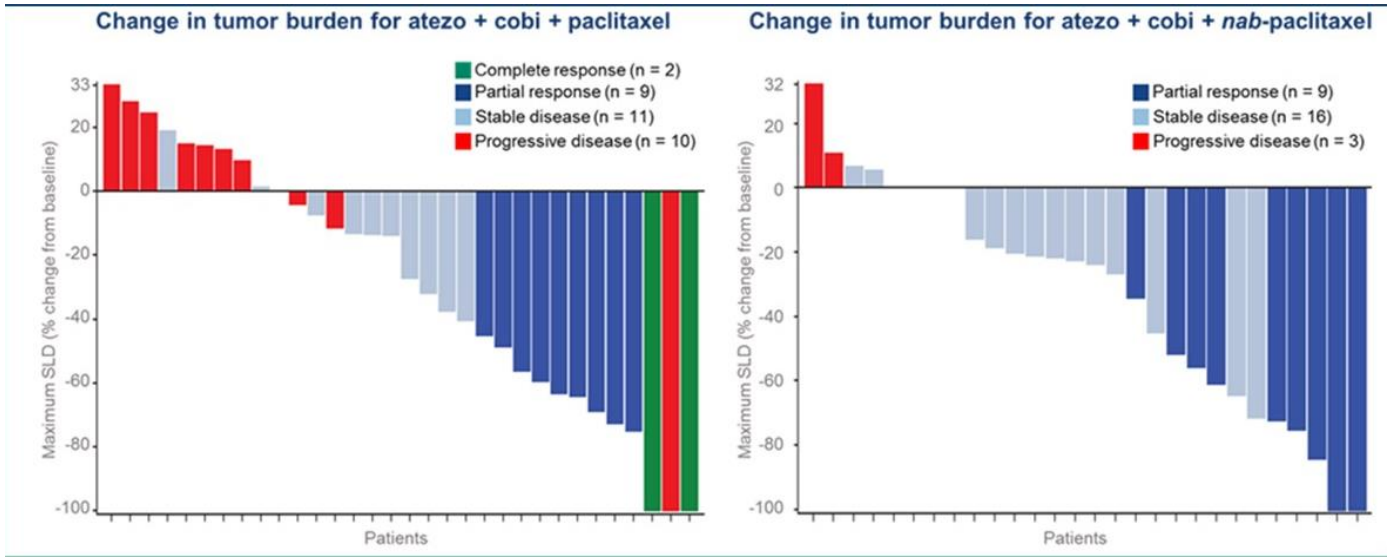
Phase II COLET study: Atezolizumab + cobimetinib + paclitaxel / nab-paclitaxel as first line treatment for patients with locally advanced or metastatic triple-negative breast cancer

Brufsky et al., (Poster #94, abstract #1013)





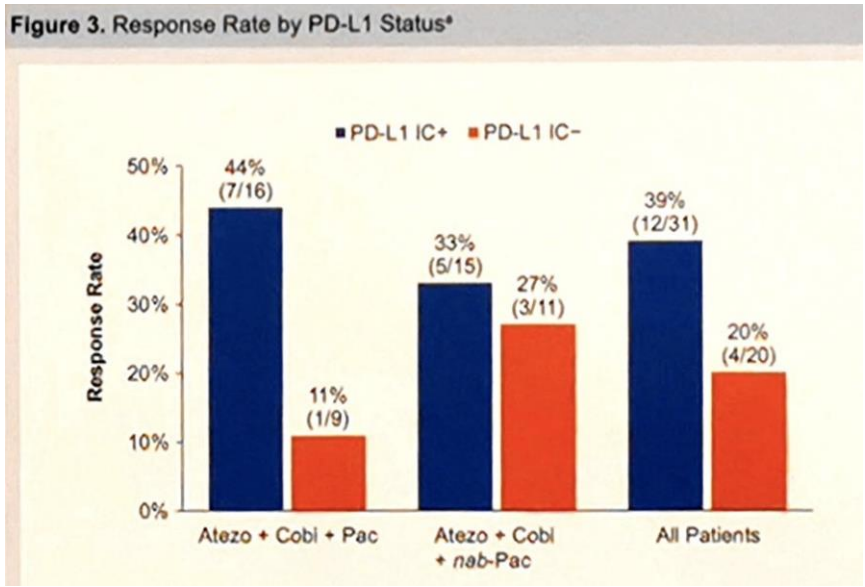


Table 4. Median PFS and OS by PD-L1 Status*

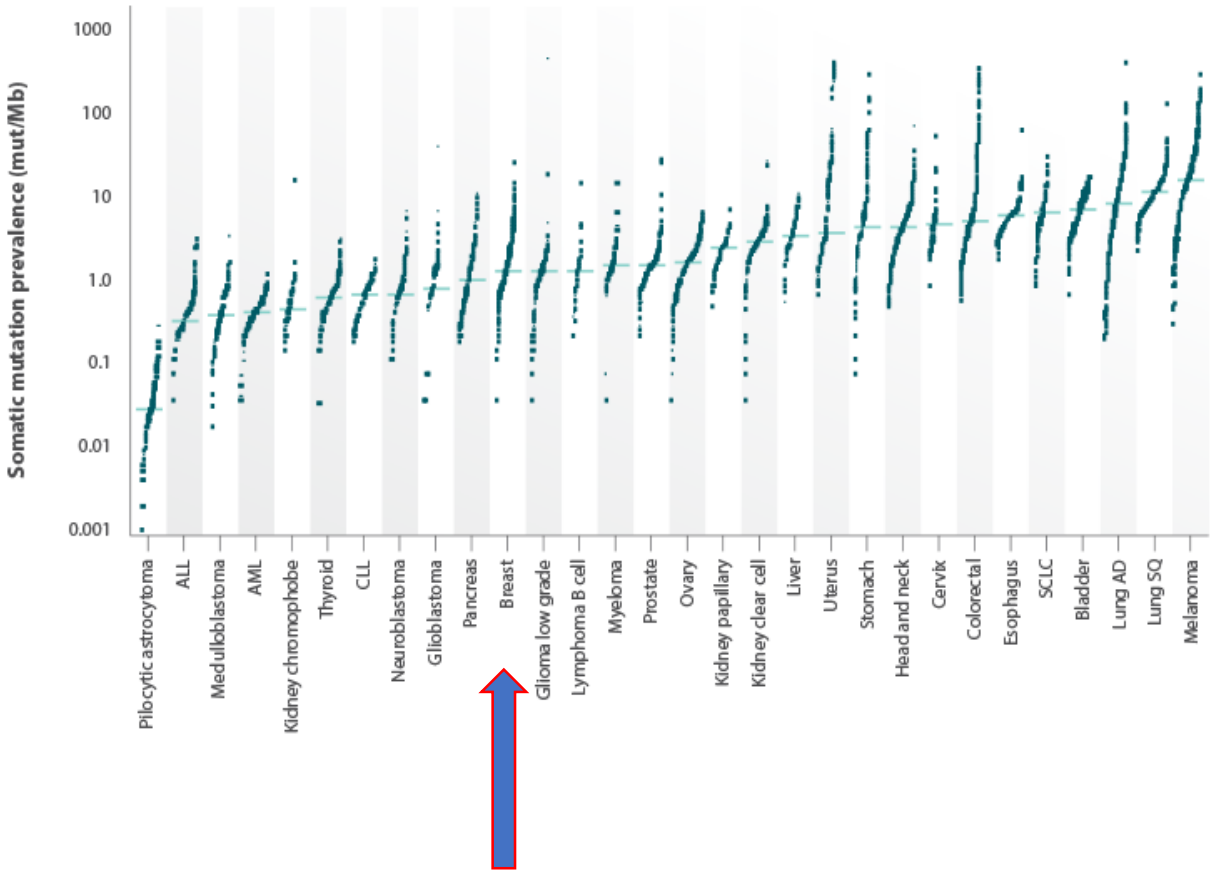
	Atezo + cobi + Pac		Atezo + cobi + *nab*-Pac	
	PD-L1- n = 9	PD-L1+ n =16	PD-L1- n = 11	PD-L1+ n =15
Median PFS, mo (95% CI)	3.7 (1.9, 5.6)	9.0 (1.9, 9.0)	5.6 (2.1, NE)	7.0 (3.7, 9.1)
Median OS, months (95% CI)	11.0 (5.5, NE)	10.5 (9.5, NE)	NE (9.4, NE)	NE (10.2, NE)

* PD-L1 IC+, ≥ 1% of tumor area containing PD-L1 stained IC; PD-L1 IC−, < 1% of tumor area containing PD-L1 stained IC.

Comparison to IMpassion130?

Is TMB a biomarker for TNBC?

Tumor mutation “hotness” of various cancers



- Breast cancer is low in the spectrum of somatic mutation preference in general
- Is TMB high breast cancer immunogenic?

Pembrolizumab in Patients with Metastatic Breast Cancer with High Tumor Mutational Burden (HTMB): Results from the Targeted Agent and Profiling Utilization Registry (TAPUR) Study

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Background

- The TAPUR Study is a phase II basket study that evaluates the anti-tumor activity of commercially available targeted agents in patients (pts) with advanced cancers with specific genomic alterations.
- Pembrolizumab (P) is an immune checkpoint inhibitor. HTMB is an emerging predictive biomarker for checkpoint inhibitor therapy. Results of a cohort of pts with metastatic breast cancer (MBC) with HTMB defined as ≥9 mutations/megabase (Muts/Mb) treated with P are reported.

Methods

Study Design:

- Eligible pts had advanced MBC with no remaining standard treatment options, PS 0-1, adequate organ function and measurable disease. Treatment was assigned according to pre-specified protocol matching rules based on genomic testing performed in CLIA-certified, CAP-accredited labs selected by clinical sites.
- Pts received P at 2 mg/kg over 30 minutes (n=8) or 200 mg (n=20) every 3 weeks (wks) until disease progression. Tumor evaluations were performed at wks 8 and 16 after treatment initiation.
- Primary endpoint is objective response (OR) or stable disease (SD) at 16+ wks per RECIST v1.1. Secondary endpoints are progression-free survival (PFS), overall survival (OS) and toxicity per CTCAE. Grades 3-5 adverse events (AEs) or serious adverse events (SAEs) at least possibly related to drug are reported.

Statistical methods:

- Simon's optimal two stage design was used to test the null hypothesis of 15% response rate versus the alternative of 35%. Power and one-sided type I error rate were set at 85% and 10%, respectively.
- Design requires 10 pts in stage I and if ≥2 pts have disease control (DC) (OR or SD at 16+ wks), the cohort is expanded to stage II with 28 pts. If ≥7 of 28 pts have DC, the drug is considered worthy of further study.

Results

- 28 pts were enrolled between October 2016 and July 2018. Baseline demographics and clinical characteristics are shown in Table 1.
- All pts in this analysis had tumors with HTMB ranging from 9 to 37 Muts/Mb as reported by a FoundationOne test (n=20) or approved by the TAPUR Molecular Tumor Board (MTB) (n=8).

Table 1: Demographics and Baseline Characteristics

Characteristic	N (%)
Median Age, years (range)	63 (36,78)
Sex	
Female	28 (100%)
Race	
White	21 (75%)
Black	6 (21%)
Asian	1 (4%)
ECOG Performance Status	
0	10 (36%)
1	18 (64%)
Prior systemic regimens	
2	1 (7%)
≥3	8 (93%)
Genomic Test Performed	
FoundationOne	20 (71%)
In house laboratory	7 (25%)
Caris MiProfile	1 (4%)

Clinical Outcomes

- DC and OR were observed in 37% and 21% of pts, respectively (Table 2). Median PFS (mPFS) and mOS are both reported in Table 2 and shown in Figure 1.
- Figure 2 shows % change from baseline in target lesions.
- There was no relationship found between PFS and Muts/Mb.
- Time on treatment among pts with response is shown in Figure 3.
- Safety was consistent with product label for P (Table 3).

Table 2: Clinical Outcomes of MBC Pts with HTMB treated with P

Clinical Outcomes	
DC (OR or SD 16+wks) N (%), [90% CI]	10 (37%), [24%, 46%]
OR (CR or PR) N (%), [95% CI]	6 (21%), [8%, 41%]
mPFS, wks, (95% CI)	10.6 (7.7, 21.1)
mOS, wks, (95% CI)	31.6 (11.9, inf)

Table 3: Total of 6 SAE/AEs at least possibly related to P experienced by 4 Pts

Grade	SAE	AEs
3	Y	colonic obstruction, hepatic failure
3	N	weight loss, hypoalbuminemia, hyponatremia
2	Y	urinary tract infection

Figure 1: OS and PFS in Advanced MBC Pts with HTMB treated with P (N=28)

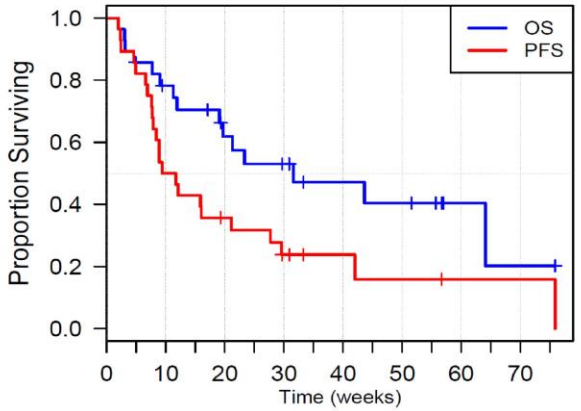


Figure 2: Best percent change from baseline in target lesion size by HER2 Status (N=28)

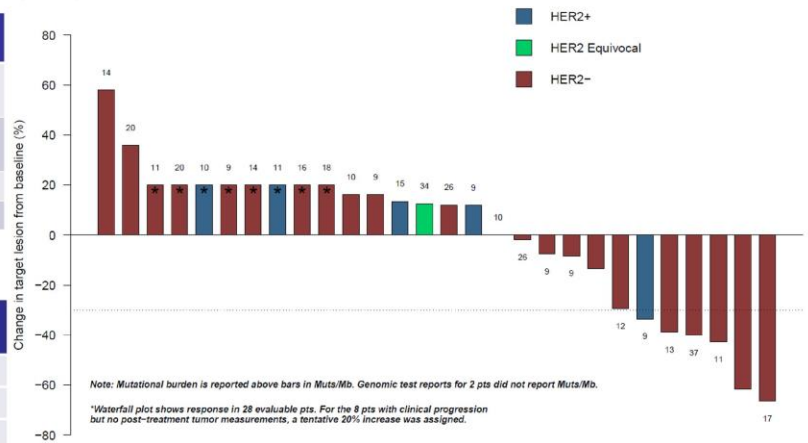
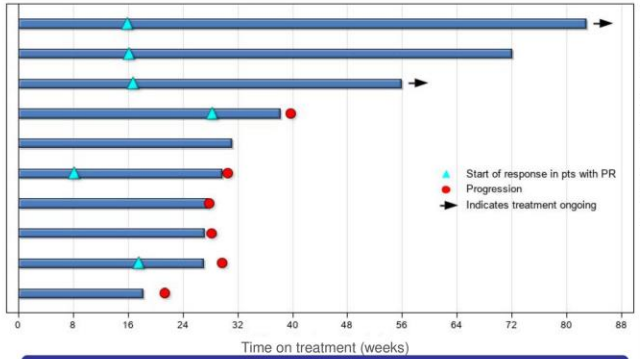


Figure 3: Time on treatment in pts with SD or objective response (N=10)



Conclusions

These results suggest monotherapy with P has anti-tumor activity in heavily pre-treated mBC pts with HTMB.

Acknowledgments

The authors would like to acknowledge the pts who participated in these cohorts as well as the following clinical lead of Merck, a TAPUR supporting pharmaceutical company: Eric Rubin, MD.

Presented By Justin Balko at 2019 ASCO Annual Meeting

- High TMB = TMB >= 9 Muts/Mb
- All metastatic breast cancer
- N = 28
- Single agent pembrolizumab
- HR status unknown
- No ‘control’

- Most response in HER2 neg cases
- Some have durable response

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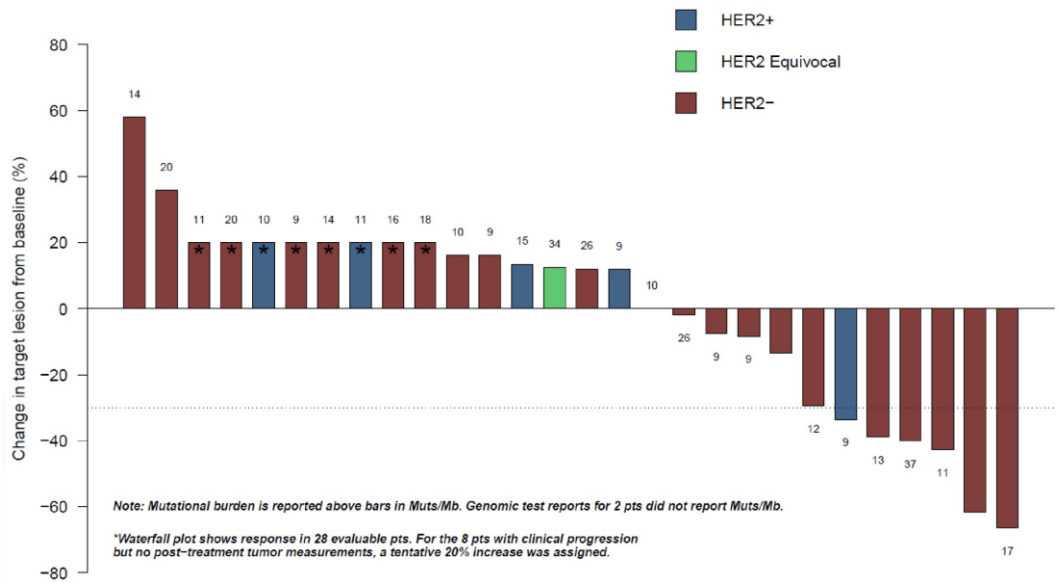

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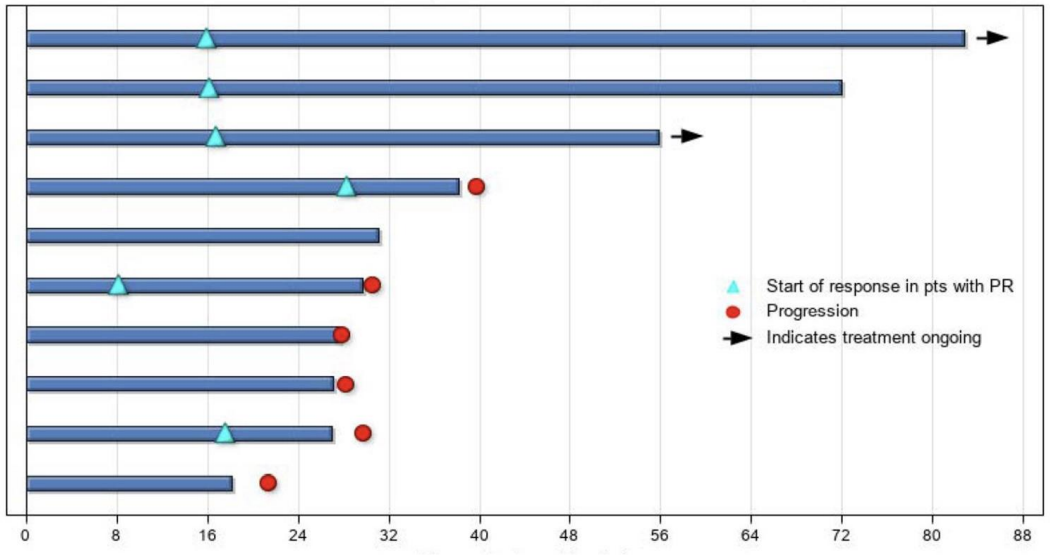

Hallmarks of Cancer: The Next Generation

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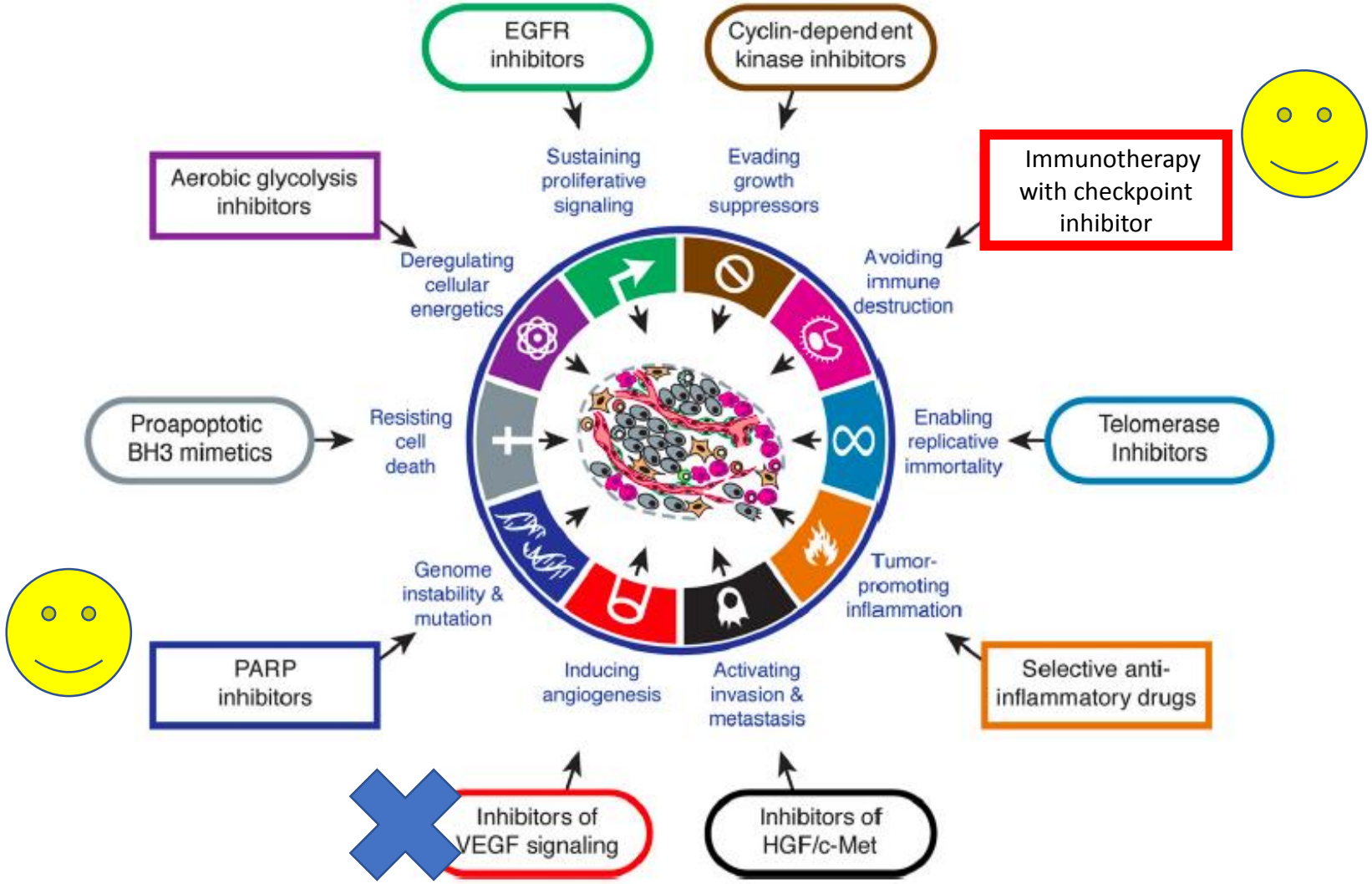

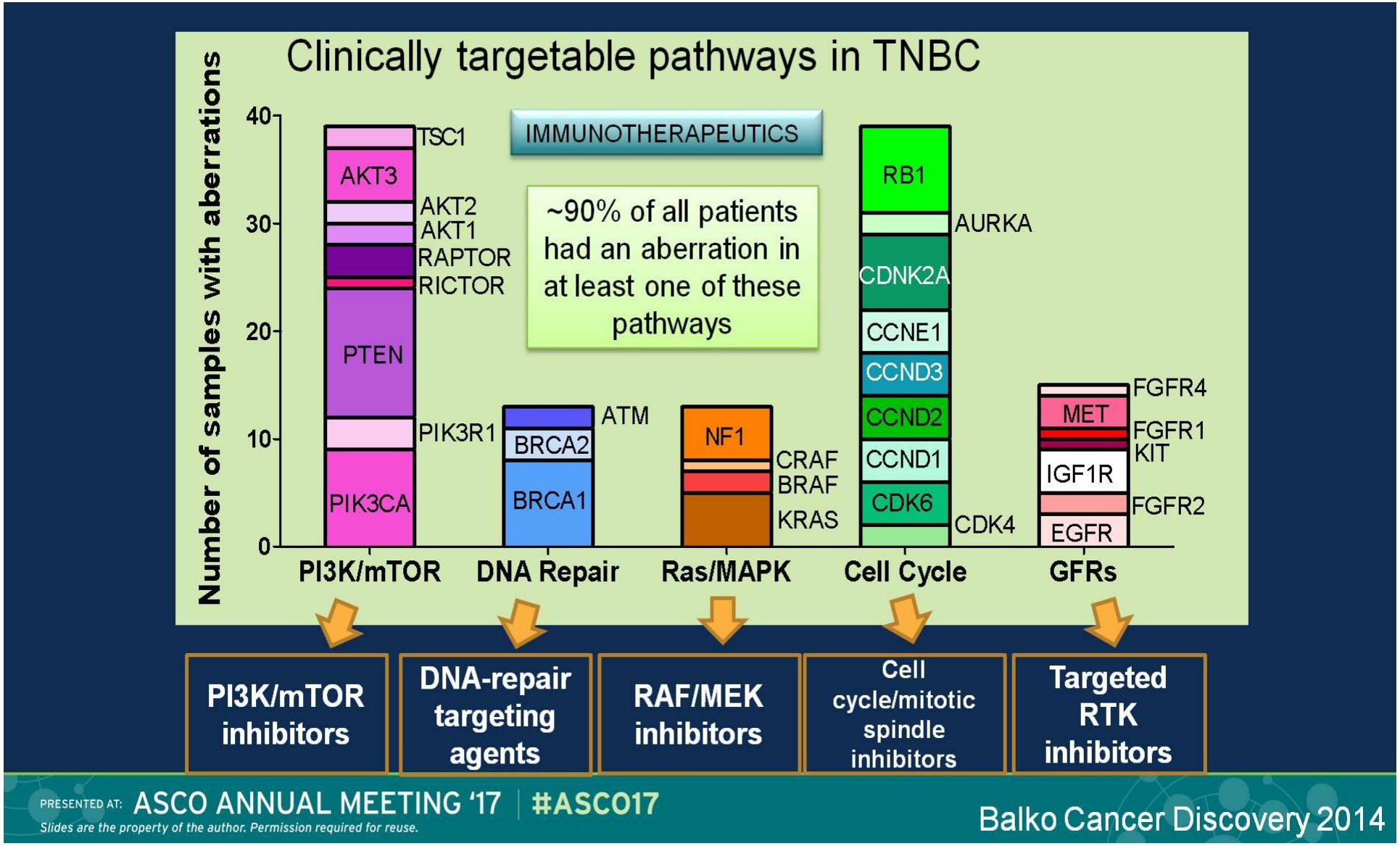

Balko Cancer Discovery 2014

Conclusion

- New therapy for TNBC in addition to chemotherapy
  - PAPR inhibitor…. For gBRCA mutation
  - Atezolizumab…. For PD-L1 IC+…. First line preferred
- Change in practice:
  - Testing of of PD-L1 IC+ in all TNBC
  - Testing of gBRCA???

Future…

- Other targeted therapies are on the rise
- Novel immunotherapy strategies
- Optimal classification system of TNBC? (Clinical, intrinsic, immune profile, mutation profile..)

Thank You