Advances in Oncology 2019: Breast Cancer Update

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October 12, 2019

Disclosures

- No relevant financial disclosures to report

Outline

Adjuvant

HER-2 positive

- KATHERINE

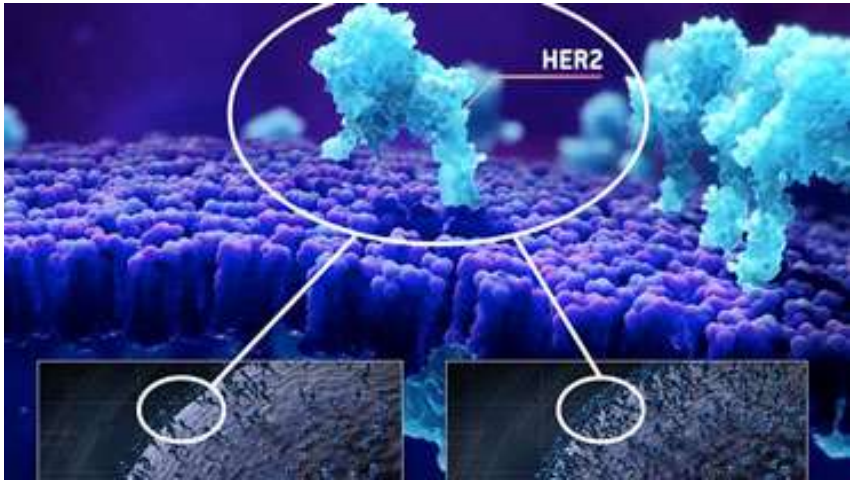
Metastatic

Hormone positive

- SOLAR-1
- MONALEESA-7

Triple negative

- IMpassion 130
- Sacituzumab govitecan-hziy



HER-2 Positive Breast Cancer

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 FEBRUARY 14, 2019 VOL. 380 NO. 7

Trastuzumab Emtansine for Residual Invasive HER2-Positive Breast Cancer

G. von Minckwitz, C.-S. Huang, M.S. Mano, S. Loibl, E.P. Mamounas, M. Untch, N. Wolmark, P. Rastogi, A. Schneeweiss, A. Redondo, H.H. Fischer, W. Jacot, A.K. Conlin, C. Arce-Salinas, I.L. Wapnir, C. Jackisch, M.P. DiGiovanna, P.A. Fasching, J.P. Crown, P. Wülfing, Z. Shao, E. Rota Caremoli, H. Wu, L.H. Lam, D. Tesarowski, M. Smitt, H. Douthwaite, S.M. Singel, and C.E. Geyer, Jr., for the KATHERINE Investigators*

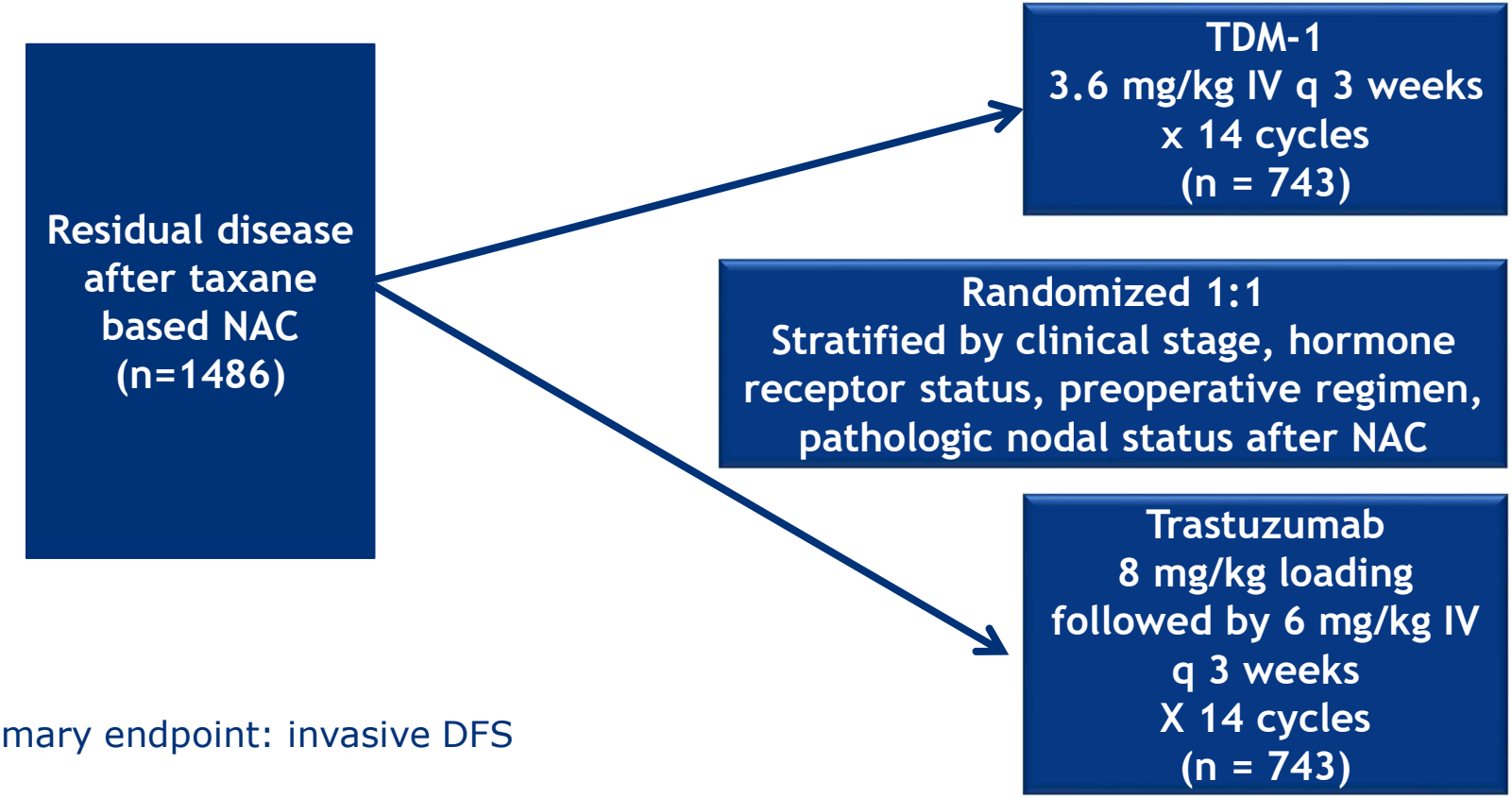
Background

- Patients who achieve pathologic complete response (PCR) with neoadjuvant chemotherapy (NAC) – improved prognosis
- Residual cancer after NAC → higher recurrence rate
- Ado-trastuzumab emtansine (TDM-1)
  - Antibody drug conjugate
  - FDA approved in metastatic setting Feb 2013

Hypothesis

- Treatment with TDM-1 vs. trastuzumab in the adjuvant setting will reduce the risk of recurrence in patients who did not achieve a PCR with NAC

KATHERINE– Trial Design



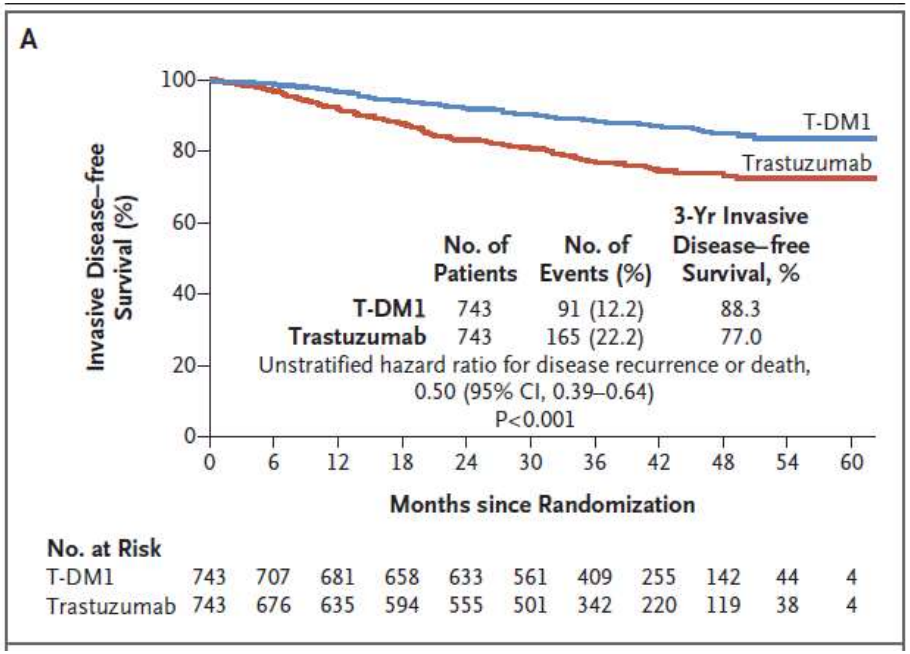
Primary endpoint: invasive DFS

Table 1. Demographic and Clinical Characteristics of the Patients at Baseline.*

Characteristic	Trastuzumab Group (N=743)	T-DM1 Group (N=743)
Median age (range) — yr	49 (23–80)	49 (24–79)
Race or ethnic group — no. of patients (%)†		
White	531 (71.5)	551 (74.2)
Asian	64 (8.6)	65 (8.7)
Black	19 (2.6)	21 (2.8)
American Indian or Alaska Native‡	50 (6.7)	36 (4.8)
Multiple or unknown	79 (10.6)	70 (9.4)
Clinical stage at presentation — no. of patients (%)		
Inoperable breast cancer§	190 (25.6)	185 (24.9)
Operable breast cancer¶	553 (74.4)	558 (75.1)
Hormone-receptor status — no. of patients (%)		
Estrogen-receptor–negative and progesterone-receptor–negative or status unknown	203 (27.3)	209 (28.1)
Estrogen-receptor–positive, progesterone-receptor–positive, or both	540 (72.7)	534 (71.9)
Previous use of anthracycline — no. of patients (%)	564 (75.9)	579 (77.9)
Neoadjuvant HER2-targeted therapy — no. of patients (%)		
Trastuzumab alone	596 (80.2)	600 (80.8)
Trastuzumab plus pertuzumab	139 (18.7)	133 (17.9)
Trastuzumab plus other HER2-targeted therapy‖	8 (1.1)	10 (1.3)

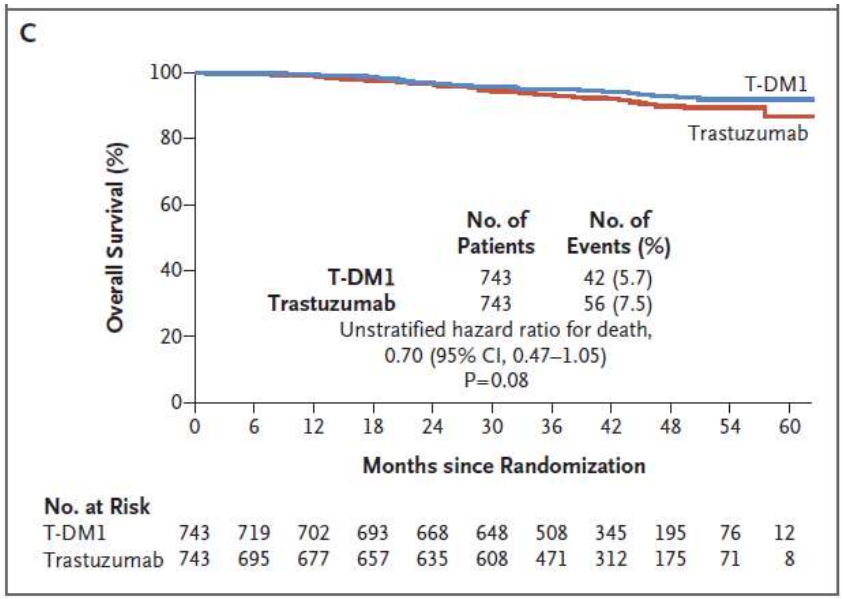
Source: Gunter von Minckwitz, M.D., Chiun-Sheng Huang, M.D., Ph.D., Max S. Mano, M.D., … William Jacot, M.D., Ph.D., et al., for the KATHERINE Investigators (2019). Trastuzumab Emtansine for Residual Invasive HER2-Positive Breast Cancer. New England Journal of Medicine, 380, 617-628.

Invasive Disease Free Survival



Source: Gunter von Minckwitz, M.D., Chiun-Sheng Huang, M.D., Ph.D., Max S. Mano, M.D., … William Jacot, M.D., Ph.D., et al., for the KATHERINE Investigators (2019). Trastuzumab Emtansine for Residual Invasive HER2-Positive Breast Cancer. New England Journal of Medicine, 380, 617-628.

Overall Survival



Source: Gunter von Minckwitz, M.D., Chiun-Sheng Huang, M.D., Ph.D., Max S. Mano, M.D., … William Jacot, M.D., Ph.D., et al., for the KATHERINE Investigators (2019). Trastuzumab Emtansine for Residual Invasive HER2-Positive Breast Cancer. New England Journal of Medicine, 380, 617-628.

Adverse Events

Table 2. Summary of Adverse Events in the Safety Population.*

Event	Trastuzumab Group (N=720)	T-DM1 Group (N=740)
	no. of patients (%)	
Any adverse event	672 (93.3)	731 (98.8)
Grade ≥3 adverse event	111 (15.4)	190 (25.7)
Adverse event leading to death†	0	1 (0.1)
Serious adverse event	58 (8.1)	94 (12.7)
Adverse event leading to discontinuation of trial drug‡	15 (2.1)	133 (18.0)
Grade ≥3 adverse event that occurred in ≥1% of patients in either group		
Decreased platelet count	2 (0.3)	42 (5.7)
Hypertension	9 (1.2)	15 (2.0)
Radiation-related skin injury	7 (1.0)	10 (1.4)
Peripheral sensory neuropathy	0	10 (1.4)
Decreased neutrophil count	5 (0.7)	9 (1.2)
Hypokalemia	1 (0.1)	9 (1.2)
Fatigue	1 (0.1)	8 (1.1)
Anemia	1 (0.1)	8 (1.1)

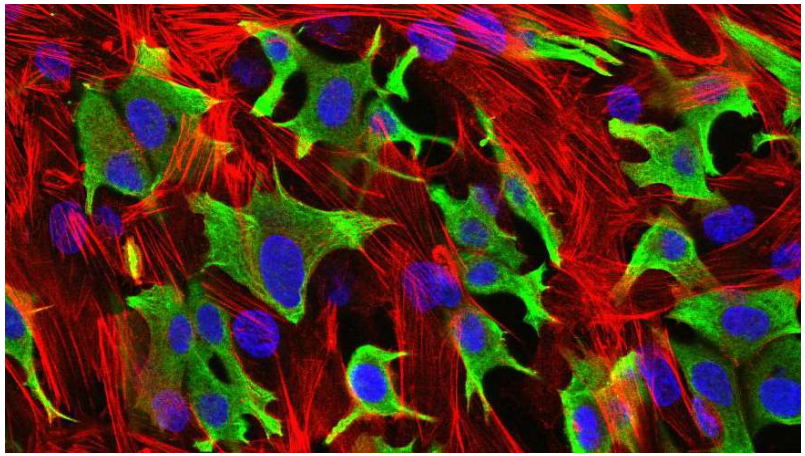
Source: Gunter von Minckwitz, M.D., Chiun-Sheng Huang, M.D., Ph.D., Max S. Mano, M.D., … William Jacot, M.D., Ph.D., et al., for the KATHERINE Investigators (2019). Trastuzumab Emtansine for Residual Invasive HER2-Positive Breast Cancer. New England Journal of Medicine, 380, 617-628.

Conclusion

- TDM-1 reduced the risk of an invasive DFS event by 50% at 3 years
  - iDFS: 88.3% with TDM-1 vs 77% with trastuzumab
- Expected toxicities with TDM-1 overall manageable

Practice Changing?

- TDM-1 FDA approved in adjuvant setting if PCR is not achieved in patients who have received NAC in May 2019



Hormone positive breast cancer

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

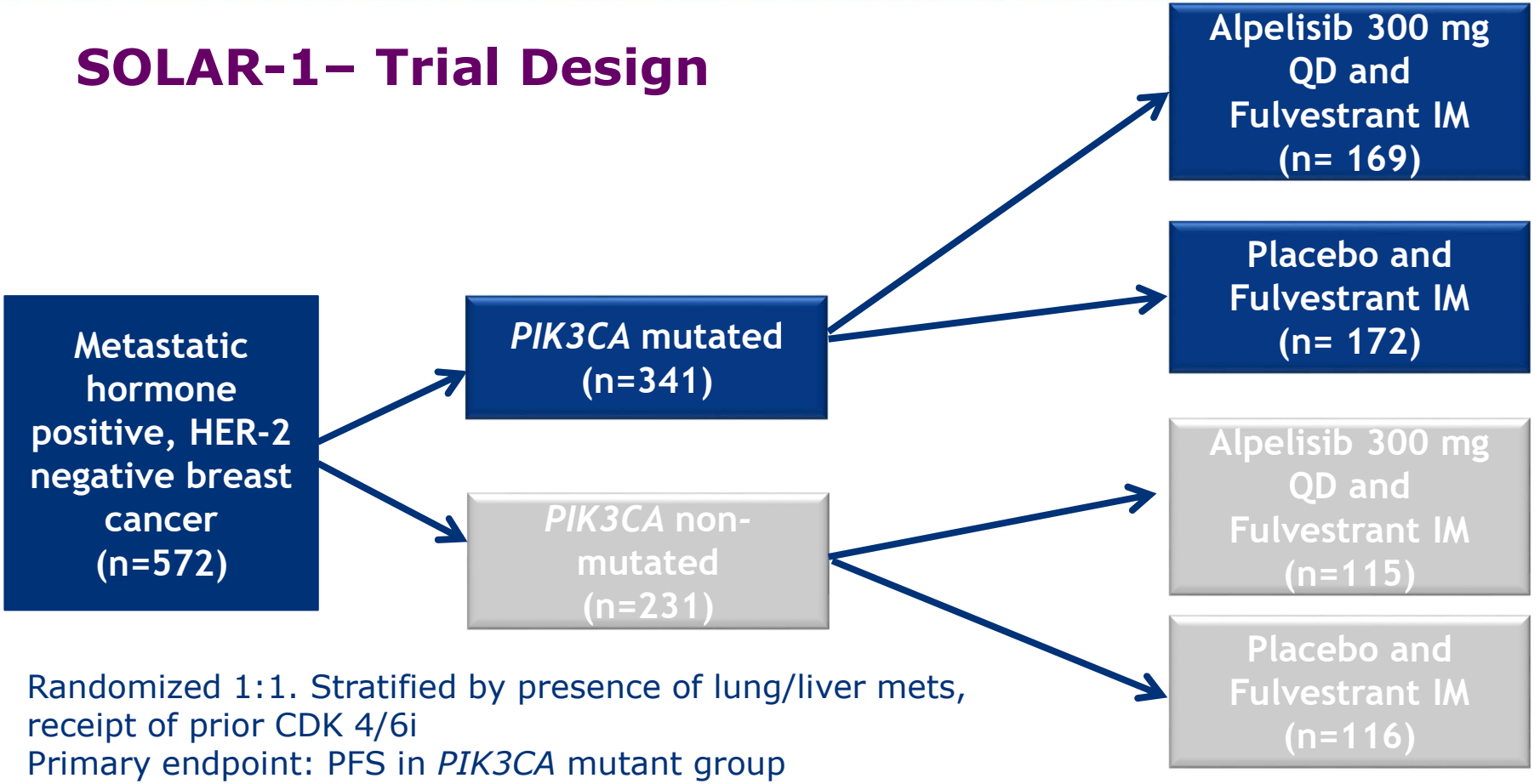
Alpelisib for *PIK3CA*-Mutated, Hormone Receptor–Positive Advanced Breast Cancer

F. André, E. Ciruelos, G. Rubovszky, M. Campone, S. Loibl, H.S. Rugo, H. Iwata, P. Conte, I.A. Mayer, B. Kaufman, T. Yamashita, Y.-S. Lu, K. Inoue, M. Takahashi, Z. Pápai, A.-S. Longin, D. Mills, C. Wilke, S. Hirawat, and D. Juric, for the SOLAR-1 Study Group*

Background

- 40% hormone positive breast cancers harbor *PIK3CA* activating mutations can cause endocrine resistance
- Alpelisib small molecular PI3K inhibitor alpha specific
  - Prior PI3K inhibitors targeted all 4 isoforms → increased toxicity
  - Alpha isoform most commonly mutated in breast cancer
- Alpelisib promising efficacy and manageable toxicities in phase I/Ib trials

SOLAR-1– Trial Design



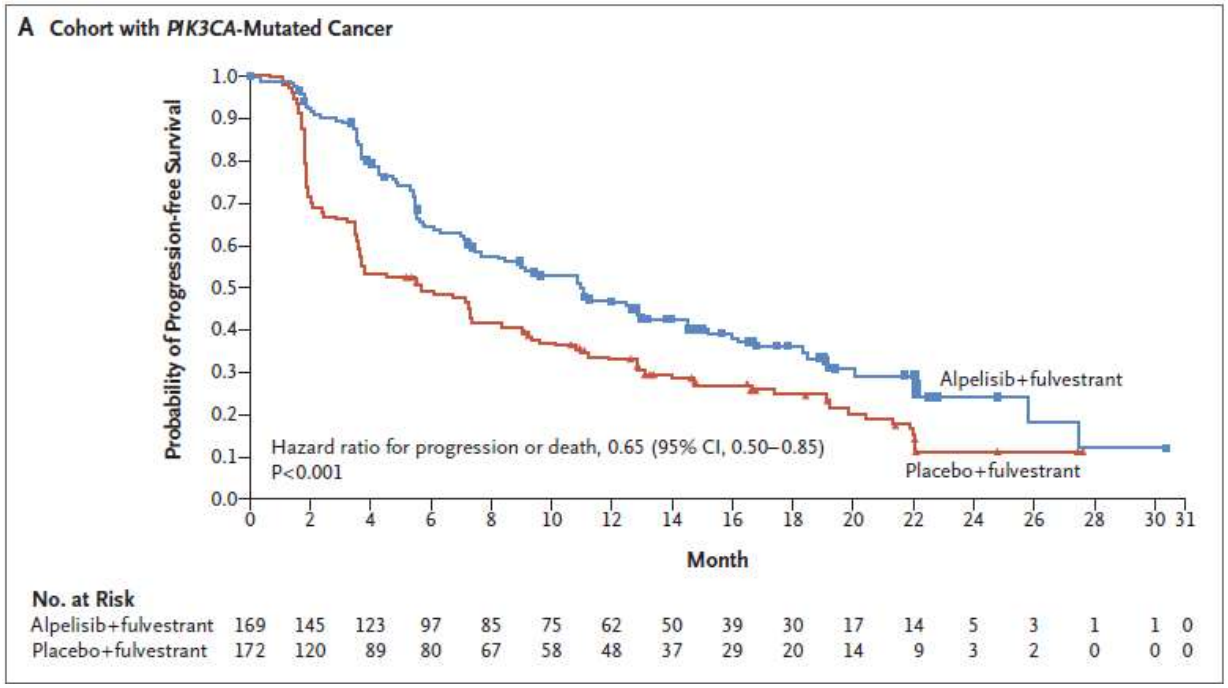
Randomized 1:1. Stratified by presence of lung/liver mets, receipt of prior CDK 4/6i
Primary endpoint: PFS in *PIK3CA* mutant group

Table 1. Characteristics of the Patients at Baseline.*

Characteristic	Cohort with *PIK3CA*-Mutated Cancer		Cohort without *PIK3CA*-Mutated Cancer	
	Alpelisib–Fulvestrant Group (N=169)	Placebo–Fulvestrant Group (N=172)	Alpelisib–Fulvestrant Group (N=115)	Placebo–Fulvestrant Group (N=116)
Age — yr				
Median	63	64	62	63
Range	25–87	38–92	39–82	32–88
Female sex — no. (%)	168 (99.4)	172 (100)	115 (100)	116 (100)
ECOG performance-status score — no. (%)†				
0	112 (66.3)	113 (65.7)	84 (73.0)	79 (68.1)
1	56 (33.1)	58 (33.7)	30 (26.1)	37 (31.9)
Missing data	1 (0.6)	1 (0.6)	1 (0.9)	0
Sites of metastases — no. (%)‡				
Breast	1 (0.6)	3 (1.7)	5 (4.3)	4 (3.4)
Bone only	42 (24.9)	35 (20.3)	26 (22.6)	23 (19.8)
Visceral site				
Any	93 (55.0)	100 (58.1)	66 (57.4)	74 (63.8)
Liver	49 (29.0)	54 (31.4)	41 (35.7)	36 (31.0)
Lung	57 (33.7)	68 (39.5)	37 (32.2)	55 (47.4)
Lung or liver	84 (49.7)	86 (50.0)	56 (48.7)	56 (48.3)
No. of metastatic sites — no. (%)				
0	0	1 (0.6)	0	0
1	63 (37.3)	52 (30.2)	44 (38.3)	33 (28.4)
2	58 (34.3)	60 (34.9)	35 (30.4)	38 (32.8)
≥3	48 (28.4)	59 (34.3)	36 (31.3)	45 (38.8)
Previous treatment — no. (%)§				
Any CDK4/6 inhibitor	9 (5.3)	11 (6.4)	7 (6.1)	8 (6.9)
Chemotherapy¶	101 (59.8)	107 (62.2)	78 (67.8)	72 (62.1)
Line of treatment in advanced disease — no. (%)‖				
First line	88 (52.1)	89 (51.7)	71 (61.7)	62 (53.4)
Second line	79 (46.7)	82 (47.7)	42 (36.5)	53 (45.7)
Endocrine status — no. (%)**				
Primary resistance	23 (13.6)	22 (12.8)	31 (27.0)	26 (22.4)
Secondary resistance	120 (71.0)	127 (73.8)	66 (57.4)	65 (56.0)
Sensitivity	20 (11.8)	19 (11.0)	16 (13.9)	20 (17.2)

Source: Fabrice André, M.D., Eva Ciruelos, M.D., Gabor Rubovszky, ... Yen-Shen Lu, M.D., et al., for the SOLAR-1 Study Group (2019). Alpelisib for PIK3CA-Mutated, Hormone Receptor–Positive Advanced Breast Cancer. New England Journal of Medicine, 380, 1929-1940.

PFS *PIK3CA* Mutated Cancer



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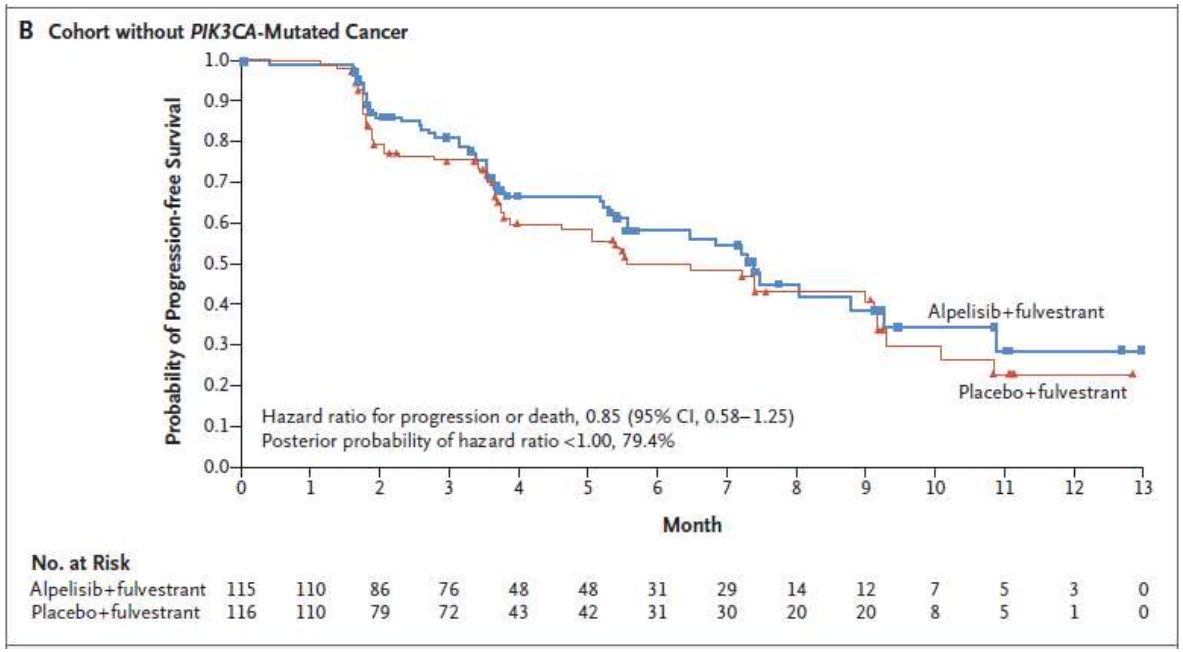
PFS *PIK3CA* Non-Mutated Cancer



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Adverse Events

Table 3. Most Frequent Adverse Events, According to Single Preferred Term and Regardless of Relationship to Intervention, in the Overall Patient Population.*

Adverse Event	Alpelisib–Fulvestrant Group (N=284)			Placebo–Fulvestrant Group (N=287)		
	Any Grade	Grade 3	Grade 4	Any Grade	Grade 3	Grade 4
	number of patients (percent)					
Any adverse event	282 (99.3)	183 (64.4)	33 (11.6)	264 (92.0)	87 (30.3)	15 (5.2)
Hyperglycemia†	181 (63.7)	93 (32.7)	11 (3.9)	28 (9.8)	1 (0.3)	1 (0.3)
Diarrhea‡	164 (57.7)	19 (6.7)	0	45 (15.7)	1 (0.3)	0
Nausea‡	127 (44.7)	7 (2.5)	0	64 (22.3)	1 (0.3)	0
Decreased appetite	101 (35.6)	2 (0.7)	0	30 (10.5)	1 (0.3)	0
Rash§	101 (35.6)	28 (9.9)	0	17 (5.9)	1 (0.3)	0
Vomiting‡	77 (27.1)	2 (0.7)	0	28 (9.8)	1 (0.3)	0
Weight loss	76 (26.8)	11 (3.9)	0	6 (2.1)	0	0
Stomatitis	70 (24.6)	7 (2.5)	0	18 (6.3)	0	0
Fatigue	69 (24.3)	10 (3.5)	0	49 (17.1)	3 (1.0)	0
Asthenia	58 (20.4)	5 (1.8)	0	37 (12.9)	0	0
Alopecia	56 (19.7)	0	0	7 (2.4)	0	0
Mucosal inflammation	52 (18.3)	6 (2.1)	0	3 (1.0)	0	0
Pruritus	51 (18.0)	2 (0.7)	0	16 (5.6)	0	0
Headache	50 (17.6)	2 (0.7)	0	38 (13.2)	0	0
Dysgeusia	47 (16.5)	0	0	10 (3.5)	0	0
Arthralgia	32 (11.3)	1 (0.4)	0	47 (16.4)	3 (1.0)	0

Source: Fabrice André, M.D., Eva Ciruelos, M.D., Gabor Rubovszky, ... Yen-Shen Lu, M.D., et al., for the SOLAR-1 Study Group (2019). Alpelisib for PIK3CA-Mutated, Hormone Receptor–Positive Advanced Breast Cancer. New England Journal of Medicine, 380, 1929-1940.

Circulating tumor DNA

- *PIK3CA* mutations evaluated in circulating blood in addition to addition to tissue samples
  - Larger PFS benefit in ctDNA *PIK3CA* mutant

Conclusion

- Alpelisib/fulvestrant prolonged PFS in patients with *PIK3CA* mutated, hormone +, HER-2 negative breast cancer
- Manageable toxicity profile
- Subgroup analysis- more effective in second line
- First drug to show benefit in a genomic subgroup in breast cancer

Practice Changing?

- Alpelisib FDA approved for metastatic *PIK3CA* mutated, hormone +, HER-2 negative breast cancer
- Implement genomic testing early on
- Potential to use ctDNA
- How to sequence with CDK 4/6i?

The NEW ENGLAND JOURNAL of MEDICINE

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Overall Survival with Ribociclib plus Endocrine Therapy in Breast Cancer

S.-A. Im, Y.-S. Lu, A. Bardia, N. Harbeck, M. Colleoni, F. Franke, L. Chow, J. Sohn, K.-S. Lee, S. Campos-Gomez, R. Villanueva-Vazquez, K.-H. Jung, A. Chakravartty, G. Hughes, I. Gounaris, K. Rodriguez-Lorenc, T. Taran, S. Hurvitz, and D. Tripathy

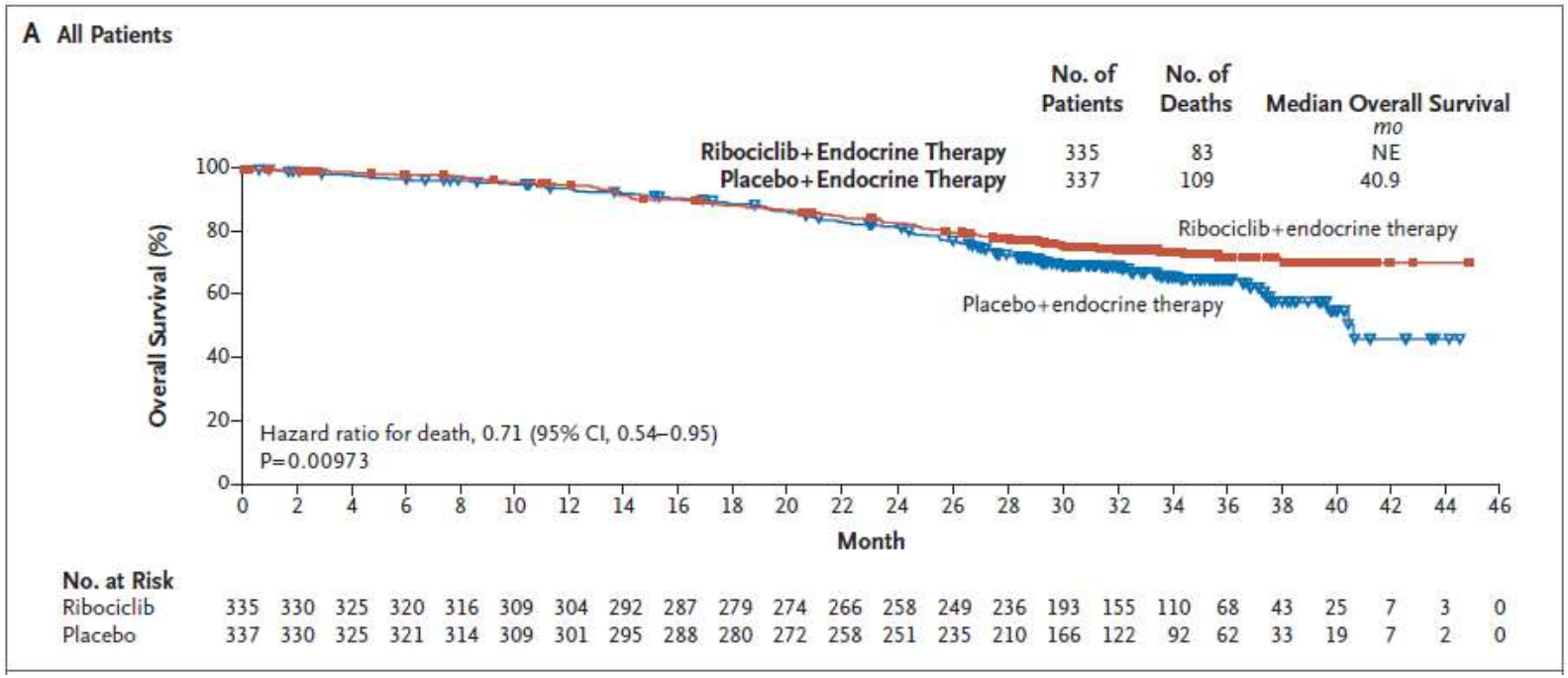
Background

- CDK 4/6i mainstay for treatment for advanced hormone positive, HER-2 negative breast cancer
  - PALOMA: palbociclib
  - MONARCH: abemaciclib
  - MONALEESA: ribociclib
- Marked PFS benefit
- OS benefit less clear

Background

- MONALEESA-7
  - 672 pre/perimenopausal women with metastatic hormone positive, HER-2 negative breast cancer
    - Goserelin and non-steroidal AI or tamoxifen with ribociclib vs placebo

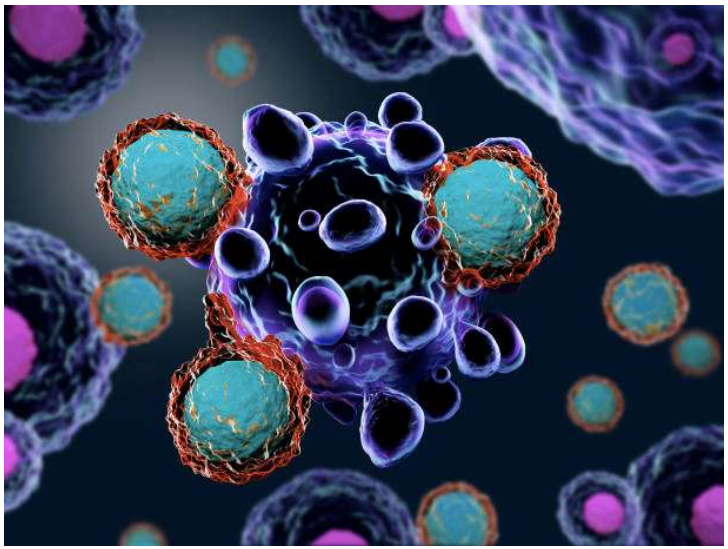
Overall survival



Source: Seock-Ah Im, M.D., Ph.D., Yen-Shen Lu, M.D., Ph.D., Aditya Bardia, M.D., …Kyung-Hae Jung, M.D., et al. (2019). Overall Survival with Ribociclib plus Endocrine Therapy in Breast Cancer. New England Journal of Medicine, 381, 307 – 316.

Summary

- First trial to show OS improvement with CDK 4/6i and endocrine therapy
- Premenopausal population
- No new concerns regarding toxicity profile



Triple Negative Breast Cancer

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

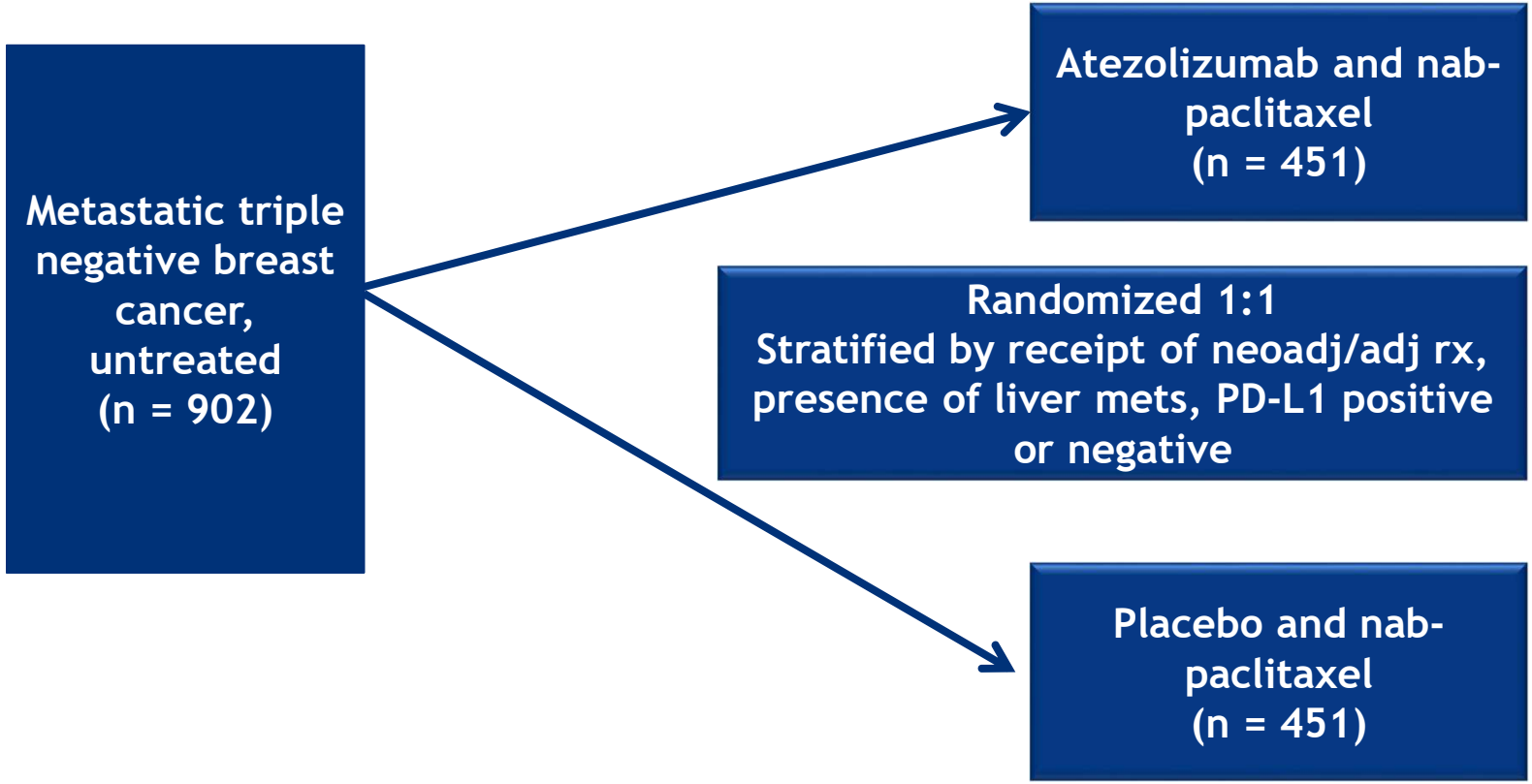
Atezolizumab and Nab-Paclitaxel in Advanced Triple-Negative Breast Cancer

P. Schmid, S. Adams, H.S. Rugo, A. Schneeweiss, C.H. Barrios, H. Iwata, V. Diéras, R. Hegg, S.-A. Im, G. Shaw Wright, V. Henschel, L. Molinero, S.Y. Chui, R. Funke, A. Husain, E.P. Winer, S. Loi, and L.A. Emens, for the IMpassion130 Trial Investigators*

Background

- TNBC aggressive molecular subtype with chemotherapy as mainstay of treatment
- Atezolizumab studied in TNBC
  - TNBC immune cell (IC) PD-L1 staining vs tumor cells (TC) has significance
  - Phase Ib trial showed efficacy with nab-paclitaxel and atezolizumab

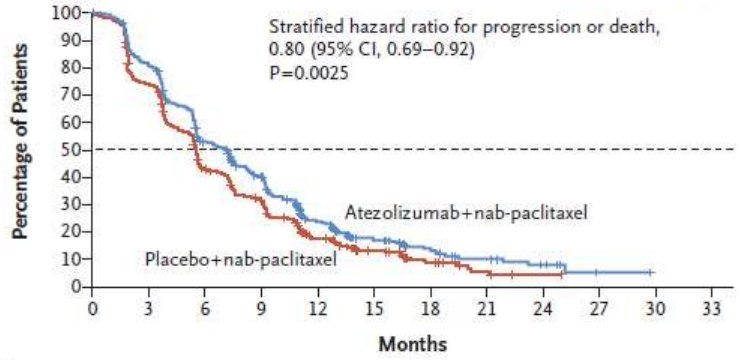
IMpassion130 – Trial Design



IMpassion 130: PFS

A Progression-free Survival in the Intention-to-Treat Population

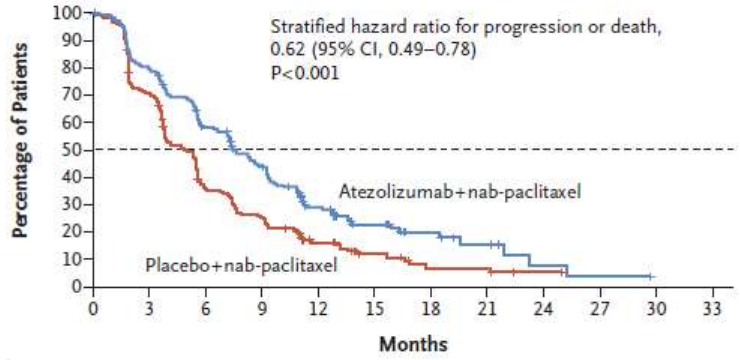
	No. of Events/ No. of Patients	Median Progression-free Survival (95% CI)	1-Yr Rate of Progression-free Survival (95% CI)
		mo	%
Atezolizumab+Nab-Paclitaxel	358/451	7.2 (5.6–7.5)	23.7 (19.6–27.9)
Placebo+Nab-Paclitaxel	378/451	5.5 (5.3–5.6)	17.7 (14.0–21.4)



No. at Risk												
Atezolizumab+ nab-paclitaxel	451	360	226	164	77	34	20	11	6	1	NE	NE
Placebo+ nab-paclitaxel	451	327	183	130	57	29	13	5	1	NE	NE	NE

B Progression-free Survival in the PD-L1–Positive Subgroup

	No. of Events/ No. of Patients	Median Progression-free Survival (95% CI)	1-Yr Rate of Progression-free Survival (95% CI)
		mo	%
Atezolizumab+Nab-Paclitaxel	138/185	7.5 (6.7–9.2)	29.1 (22.2–36.1)
Placebo+Nab-Paclitaxel	157/184	5.0 (3.8–5.6)	16.4 (10.8–22.0)



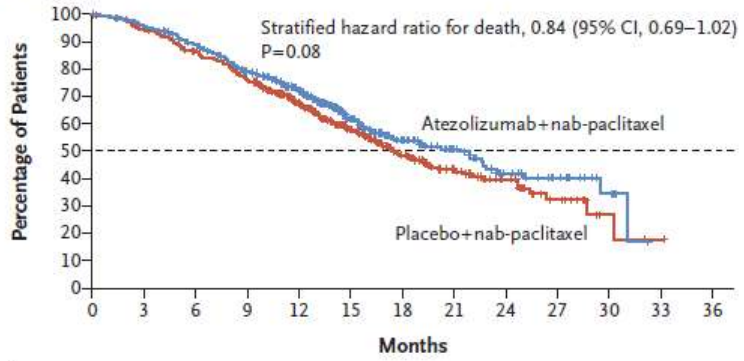
No. at Risk												
Atezolizumab+ nab-paclitaxel	185	146	104	75	38	19	10	6	2	1	NE	NE
Placebo+ nab-paclitaxel	184	127	62	44	22	11	5	5	1	NE	NE	NE

Source: Schmid, P., Adams, S., Rugo, H. S., Schneeweiss, A., Barrios, C. H., Iwata, H., … Emens, L. A. (2018). Atezolizumab and Nab-Paclitaxel in Advanced Triple-Negative Breast Cancer. New England Journal of Medicine, 379(22), 2108–2121.

IMpassion 130: OS

C Overall Survival in the Intention-to-Treat Population

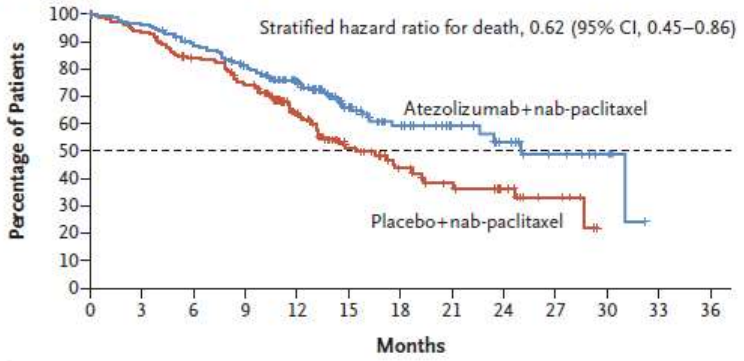
	No. of Events/ No. of Patients	Median Overall Survival (95% CI)	2-Yr Rate of Overall Survival (95% CI)
		mo	%
Atezolizumab+Nab-Paclitaxel	181/451	21.3 (17.3–23.4)	42.1 (34.3–49.9)
Placebo+Nab-Paclitaxel	208/451	17.6 (15.9–20.0)	39.7 (33.2–46.3)



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

D Overall Survival in the PD-L1–Positive Subgroup

	No. of Events/ No. of Patients	Median Overall Survival (95% CI)	2-Yr Rate of Overall Survival (95% CI)
		mo	%
Atezolizumab+Nab-Paclitaxel	64/185	25.0 (22.6–NE)	53.5 (42.3–64.6)
Placebo+Nab-Paclitaxel	88/184	15.5 (13.1–19.4)	36.6 (26.4–46.7)



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

Source: Schmid, P., Adams, S., Rugo, H. S., Schneeweiss, A., Barrios, C. H., Iwata, H., … Emens, L. A. (2018). Atezolizumab and Nab-Paclitaxel in Advanced Triple-Negative Breast Cancer. New England Journal of Medicine, 379(22), 2108–2121.

IMpassion 130: Adverse Events

Table 3. Key Adverse Events.*

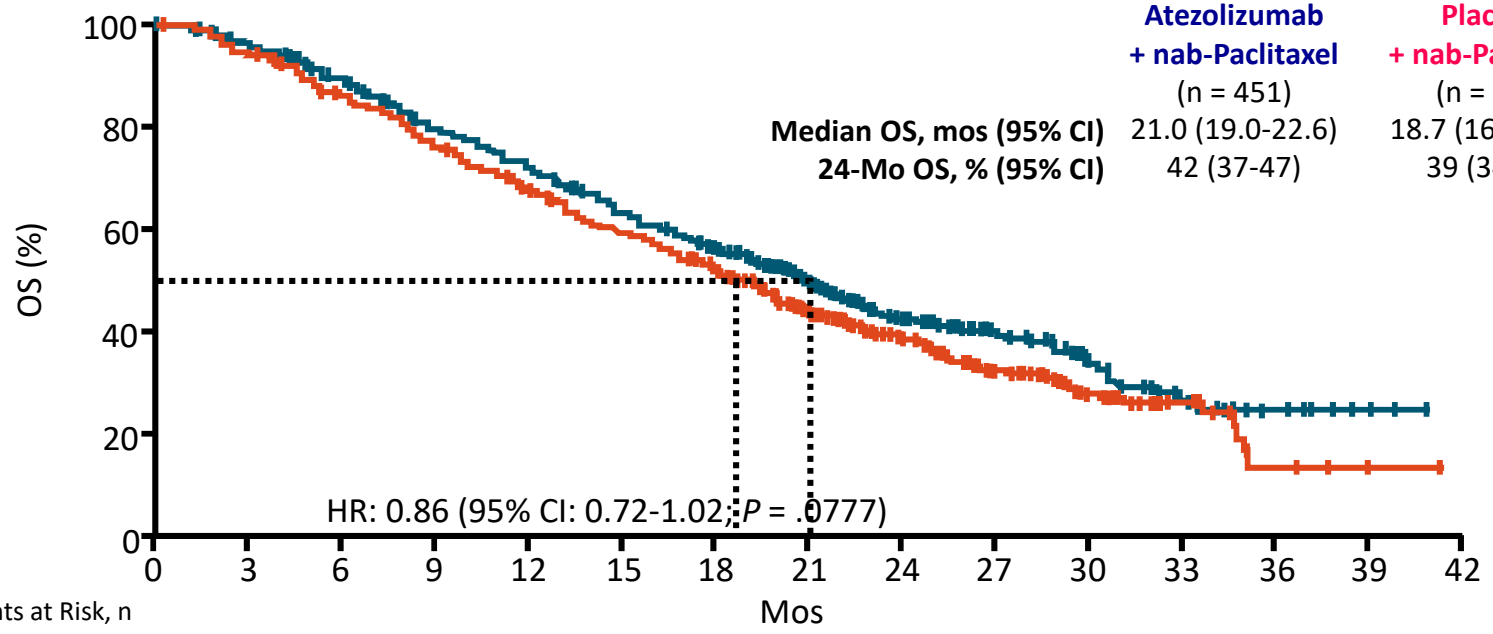
Event	Atezolizumab + Nab-Paclitaxel (N=452)		Placebo + Nab-Paclitaxel (N=438)	
	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4
	number of patients with event (percent)			
Alopecia	255 (56.4)	3 (0.7)	252 (57.5)	1 (0.2)
[redacted]				
Cough	112 (24.8)	0	83 (18.9)	0
Peripheral neuropathy	98 (21.7)	25 (5.5)	97 (22.1)	12 (2.7)
[redacted]				
Pyrexia	85 (18.8)	3 (0.7)	47 (10.7)	0
Hypothyroidism	62 (13.7)	0	15 (3.4)	0

Source: Schmid, P., Adams, S., Rugo, H. S., Schneeweiss, A., Barrios, C. H., Iwata, H., … Emens, L. A. (2018). Atezolizumab and Nab-Paclitaxel in Advanced Triple-Negative Breast Cancer. New England Journal of Medicine, 379(22), 2108–2121.

IMpassion130

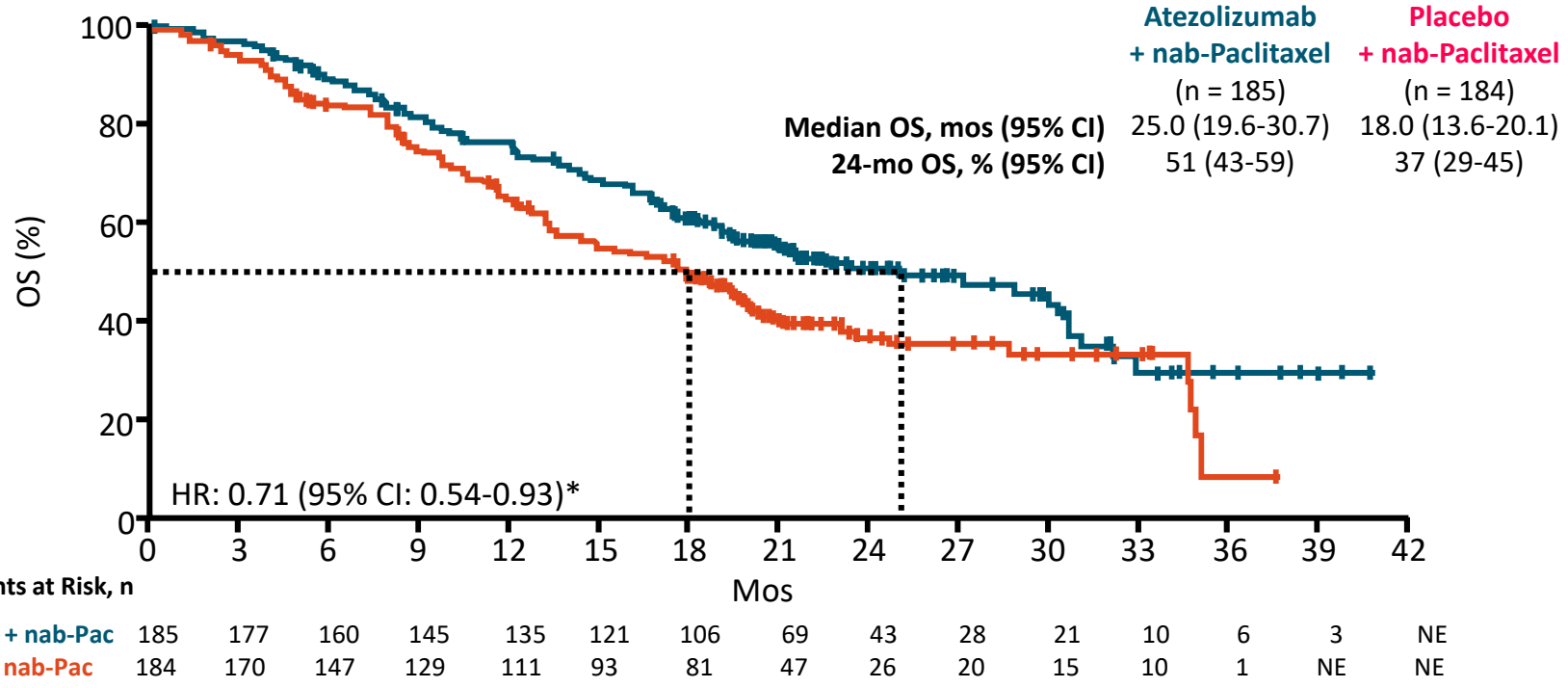
- FDA approved atezolizumab with nab-paclitaxel, along with Ventana Medical Systems' SP142 PD-L1 IHC assay as companion diagnostic test to identify PD-L1 IC ≥ 1% in March 2019
- ASCO 2019 Updated OS Analysis
  - Second interim OS: median f/u time 18 months

IMpassion130 Update: OS in ITT Population



Source: clinicaloptions.com

IMpassion130 Update: OS in PD-L1+ Subgroup

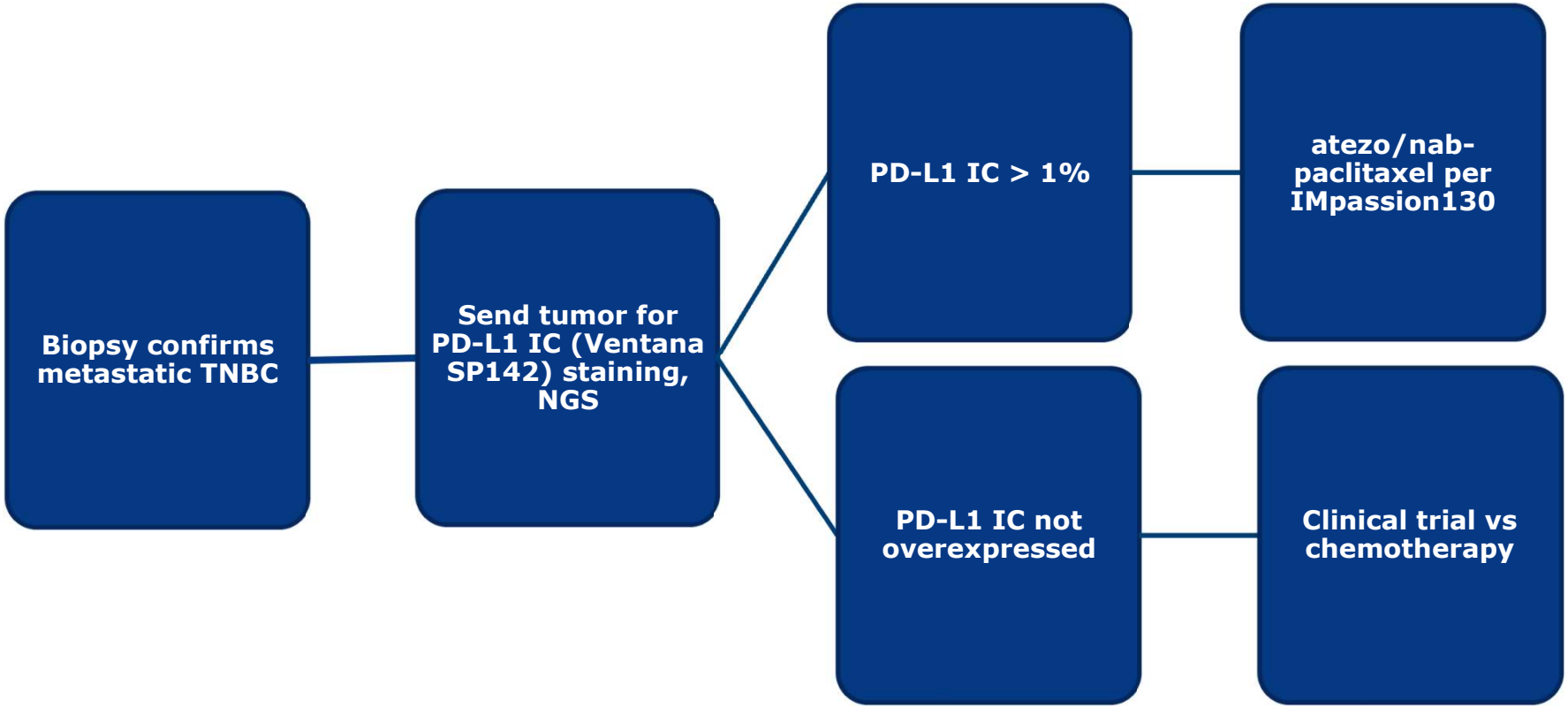


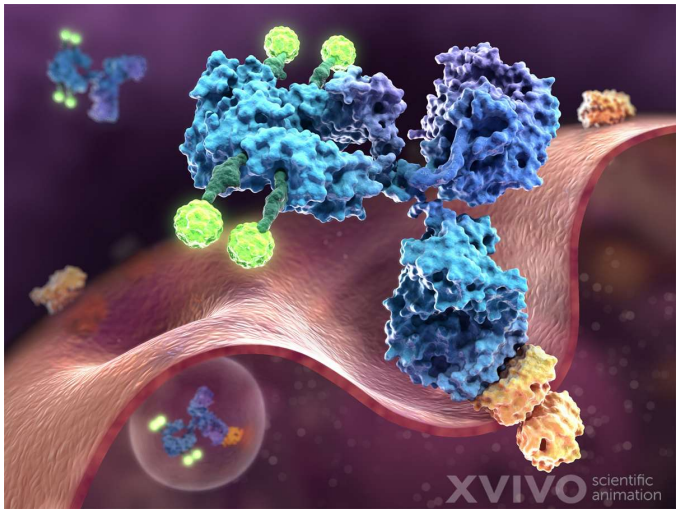
Source: clinicaloptions.com

IMpassion 130: Biomarker Analysis

- 15% patients *BRCA* mutated
  - PD-L1 IC negative group: no association between treatment and survival noted
  - PD-L1 IC positive group: significant benefit of PFS and OS
  - Small numbers
- PD-L1 IC
  - PD-L1 IC most predictive of atezolizumab/nab-paclitaxel efficacy on PFS and OS with expression > 1%

Therapeutic Algorithm in TNBC





Antibody-drug conjugate

Sacituzumab govitecan-hziy

- Antibody drug conjugate: human trophoblast cell-surface antigen 2 (Trop-2) with SN-38 (topoisomerase-I inhibitor)
  - Trop-2 overexpressed in many epithelial cells including up to 85% of TNBC
  - SN-38 released intracellularly and in tumor microenvironment
- IMMU-132-01
  - Phase I/II open label, multi-center, basket design, single group trial
  - Prelim data reported on 69 pts TNBC who rec'd at least 1 prior line of therapy (J Clin Oncol 2017; 35: 2141-8)
  - Breakthrough therapy designation by FDA for TNBC patients in Feb 2016 who had rec'd at least 2 prior lines of therapy
  - NEJM Feb 2019 reporting on patients rec'd as third line or beyond in metastatic TNBC

Metastatic triple negative breast cancer, at least 2 prior lines (n = 108) → **Sacituzumab govitecan-hziy 10 mg/kg IV on days 1, 8 of 21 day cycle (n= 108)**

Endpoints:
Primary- ORR (objective response rate)
Secondary- TTR, DOR, CBR, PFS, OS

Baseline Characteristics

Table 1. Characteristics of the Patients at Baseline.

Characteristic	Patients (N=108)
Sex — no. (%)	
Female	107 (99.1)
Male	1 (0.9)
Median age (range) — yr	55 (31–80)
Race or ethnic group — no. (%)*	
White	82 (75.9)
Black	8 (7.4)
Asian	3 (2.8)
Other or not specified†	15 (13.9)
ECOG performance-status score — no. (%)‡	
0	31 (28.7)
1	77 (71.3)
[redacted]	
Previous use of taxanes or anthracyclines for metastatic or nonmetastatic disease — no. (%)	
[redacted]	
Previous use of chemotherapy drugs for metastatic disease — no. (%)	
Cyclophosphamide	20 (18.5)
Platinum agents	74 (68.5)
Gemcitabine	59 (54.6)
Fluoropyrimidine agents	56 (51.9)
Eribulin	49 (45.4)
Vinorelbine	17 (15.7)
[redacted]	

Source: Bardia, A., Mayer, I. A., Vahdat, L. T., Tolaney, S. M., Isakoff, S. J., Diamond, J. R., … Kalinsky, K. (2019). Sacituzumab Govitecan-hziy in Refractory Metastatic Triple-Negative Breast Cancer. New England Journal of Medicine, 380(8), 741–751.

Adverse Events

Table 2. Summary of Adverse Events in Patients Receiving Sacituzumab Govitecan-hziy.*

Adverse Event	Patients (N=108)		
	Any Grade	Grade 3	Grade 4
	number of patients with event (percent)		
Any adverse event	108 (100)	71 (66)	21 (19)
Gastrointestinal disorders	102 (94)	21 (19)	0
Nausea	72 (67)	7 (6)	0
[redacted]			
Vomiting	53 (49)	7 (6)	0
Constipation	37 (34)	1 (1)	0
Abdominal pain†	27 (25)	1 (1)	0
Mucositis‡	15 (14)	0	0
General disorders and administration-site conditions	82 (76)	10 (9)	0
Fatigue and asthenia	59 (55)	9 (8)	0
Peripheral edema	17 (16)	0	0
Pyrexia	13 (12)	0	0
Blood and lymphatic system disorders	80 (74)	25 (23)	15 (14)
[redacted]			

Source: Bardia, A., Mayer, I. A., Vahdat, L. T., Tolaney, S. M., Isakoff, S. J., Diamond, J. R., … Kalinsky, K. (2019). Sacituzumab Govitecan-hziy in Refractory Metastatic Triple-Negative Breast Cancer. New England Journal of Medicine, 380(8), 741–751.

Results

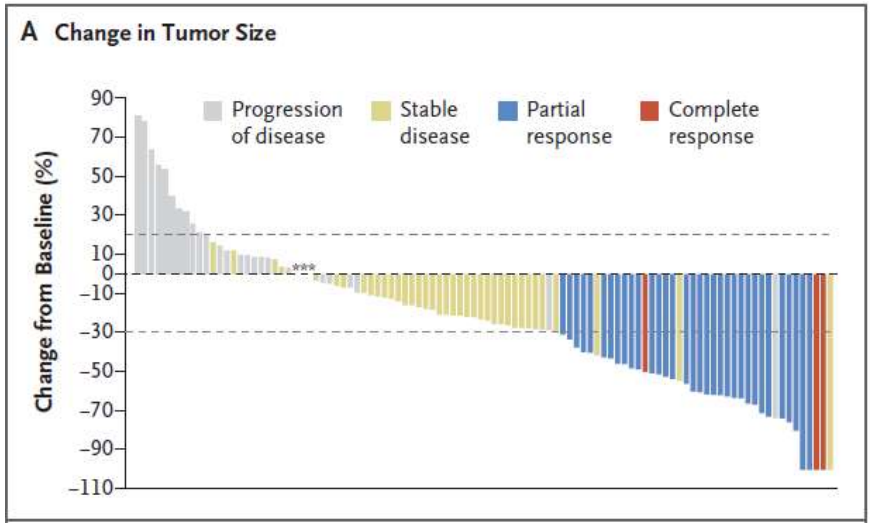
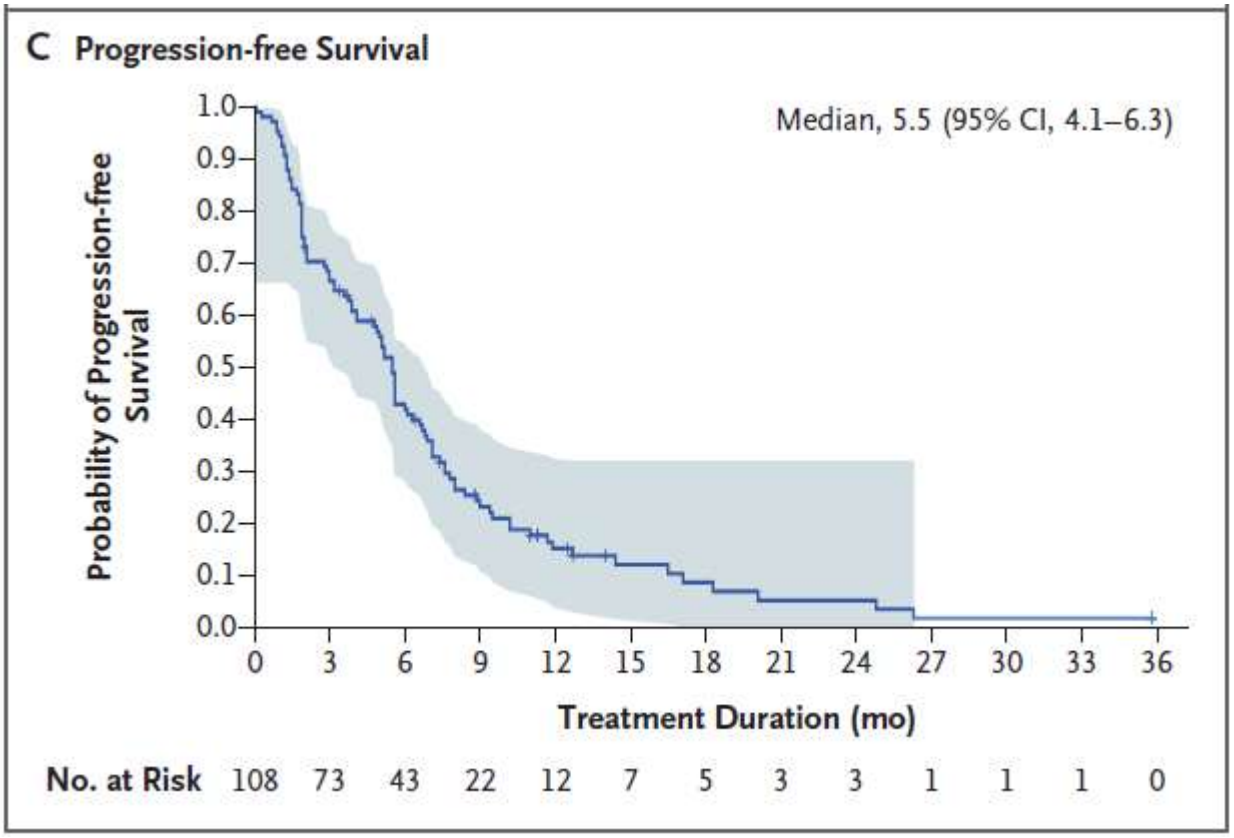


Table 3. Summary of Treatment Efficacy, According to Local Assessment.

Variable	Patients (N=108)
[redacted]	
[redacted]	
Stable disease — no. of patients (%)	40 (37.0)
Progressive disease — no. of patients (%)	28 (25.9)
Not evaluated — no. of patients (%)*	4 (3.7)
[redacted]	
[redacted]	
[redacted]	

Source: Bardia, A., Mayer, I. A., Vahdat, L. T., Tolaney, S. M., Isakoff, S. J., Diamond, J. R., … Kalinsky, K. (2019). Sacituzumab Govitecan-hziy in Refractory Metastatic Triple-Negative Breast Cancer. New England Journal of Medicine, 380(8), 741–751.


C Progression-free Survival
Median, 5.5 (95% CI, 4.1–6.3)
Probability of Progression-free Survival
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
0 3 6 9 12 15 18 21 24 27 30 33 36
Treatment Duration (mo)
No. at Risk 108 73 43 22 12 7 5 3 3 1 1 1 0

Summary

- Sacituzumab govitecan-hziy – novel MOA with efficacy in heavily pretreated TNBC
  - ORR 33.3%
  - Median PFS 5.5 months
- Overall manageable safety profile
  - Bone marrow, GI

Practice changing?

- FDA rejected in Jan 2019
  - Manufacturing facility issues
- FDA approval in 2020?
  - Phase III ASCENT trial for TNBC
  - HR+, HER-2 negative similar efficacy as seen w/TNBC

Take Home Points

- Increasing data to support the use of NAC in HER-2 positive breast cancer- escalate adjuvant therapy in diseases that do not achieve a PCR
  - TNBC- CREATE-X
- Next generation sequencing early on to assess for targetable mutation in the advanced setting
  - *PIK3CA* mutations → Alpelisib
- PD-L1 staining up front for metastatic TNBC
- Clinical trial whenever possible!

Thank you!