UNIVERSITÀ DEL PIEMONTE ORIENTALE

Ruolo di *Nab*-paclitaxel nella malattia metastatica

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Novara

Nab-paclitaxel Perspectives

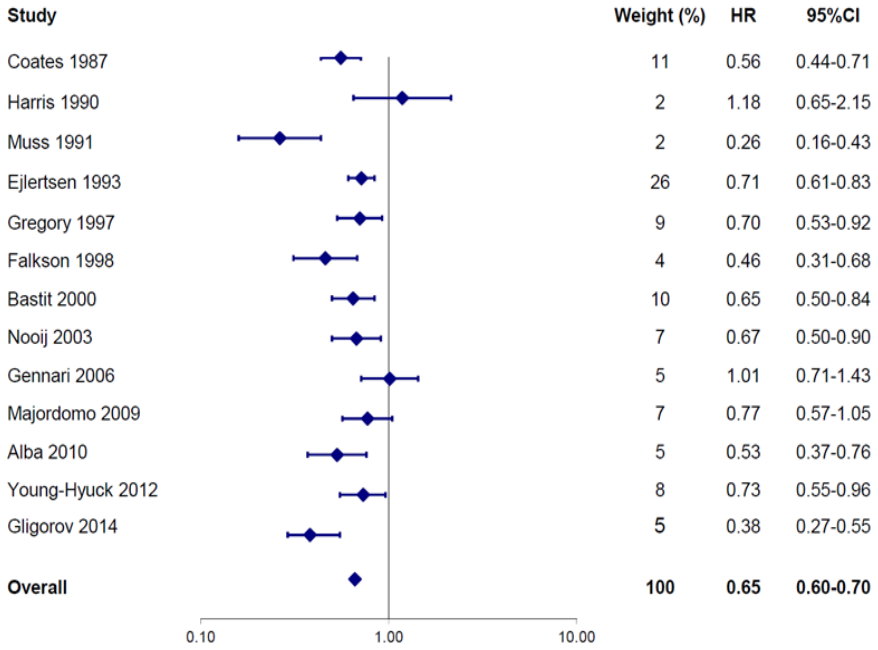
- ❑ Elderly patients
- ❑ Maintenance
- ❑ Triple negative patients
- ❑ Immuno-Oncology combinations

Maintenance Therapy in MBC

Study	Pts	Comparison	PFS, *p*	OS, *p*
Coates 1987	305	3 AC or CMF vs AC or CMF (PD)	.02	ns
Harris 1990	43	4 Mitox vs Mitox (PD)	ns	ns
Muss 1991	145	6 FAC vs 6 FAC→ 12 CMF	.001	ns
Ejlertsen 1993	318	8 FEC vs 24 FEC	.003	.03
Gregory 1997	100	6 VA(E)C/MMM vs 12 VA(E)C/MMM	.001	ns
Falkson 1998	195	6 Doxo vs 6 Doxo → CMF (PD)	.0001	ns
Bastit 2000	417	4 FEC vs 11/12 FEC	.003	ns
Nooij 2003	196	6 CMF vs CMF (PD)	.01	ns
Gennari 2006	215	ETx 8 vs ETx 8 → 3wTXL x 8	ns	ns
Mayordomo 2009	180	E x 3 → 3TXL vs E x 3 → 3TXL → wTXL (PD)	ns	ns
Alba 2010	155	6 AT vs 6 AT→ PLD (PD)	.0005	ns
Young-Hyuck 2012	231	6 PG vs PG (PD)	0.031	0.048
Gligorov 2014	185	4/6 TXT vs 4/6 TXT →Cape (PD) +B	<0.001	<0.001

Maintenance CT: Metanalysis

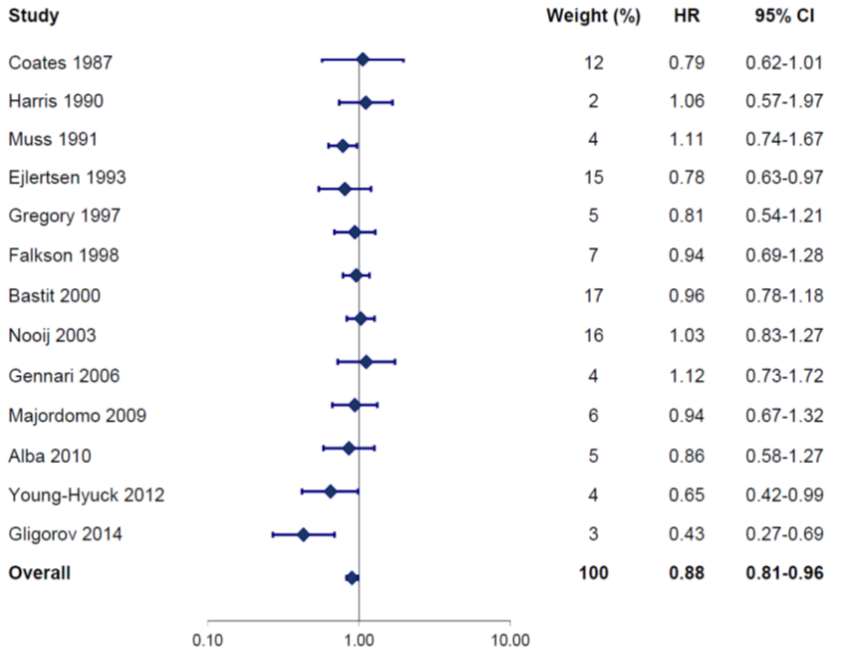
Progression Free Survival



Test of heterogeneity I^2= 70%, p <0,001

Test of treatment ent effect = p < 0,001

Overall Survival



Test of heterogeneity I^2= 35%, p =0,09

Test of treatment ent effect p = 0,003

SNAP

Schedules of nab-Paclitaxel

IBCSG 42-12 / BIG 2-12

Coordinating Group: IBCSG

Pharma Partner: Celgene

Study Chair: Alessandra Gennari
Ann Oncol, 2018

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SNAP (IBCSG 42-12 / BIG 2-12)

Title: A randomized phase II study evaluating different schedules of nab-Paclitaxel in metastatic breast cancer (SNAP Trial)

Patient Population: Patients with histologically or cytologically confirmed HER2-negative metastatic (stage IV) breast cancer who have not received chemotherapy for metastatic breast cancer.

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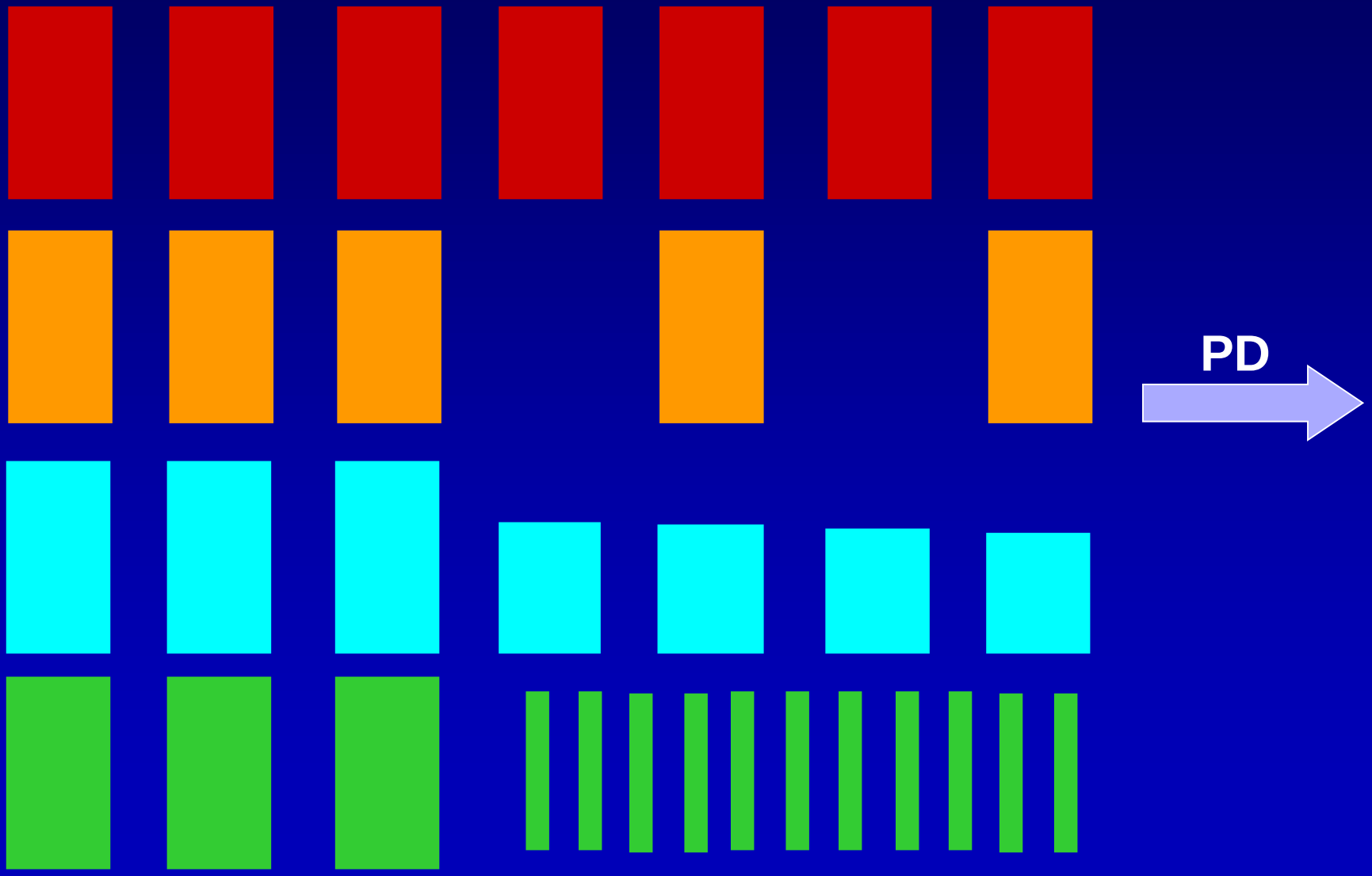
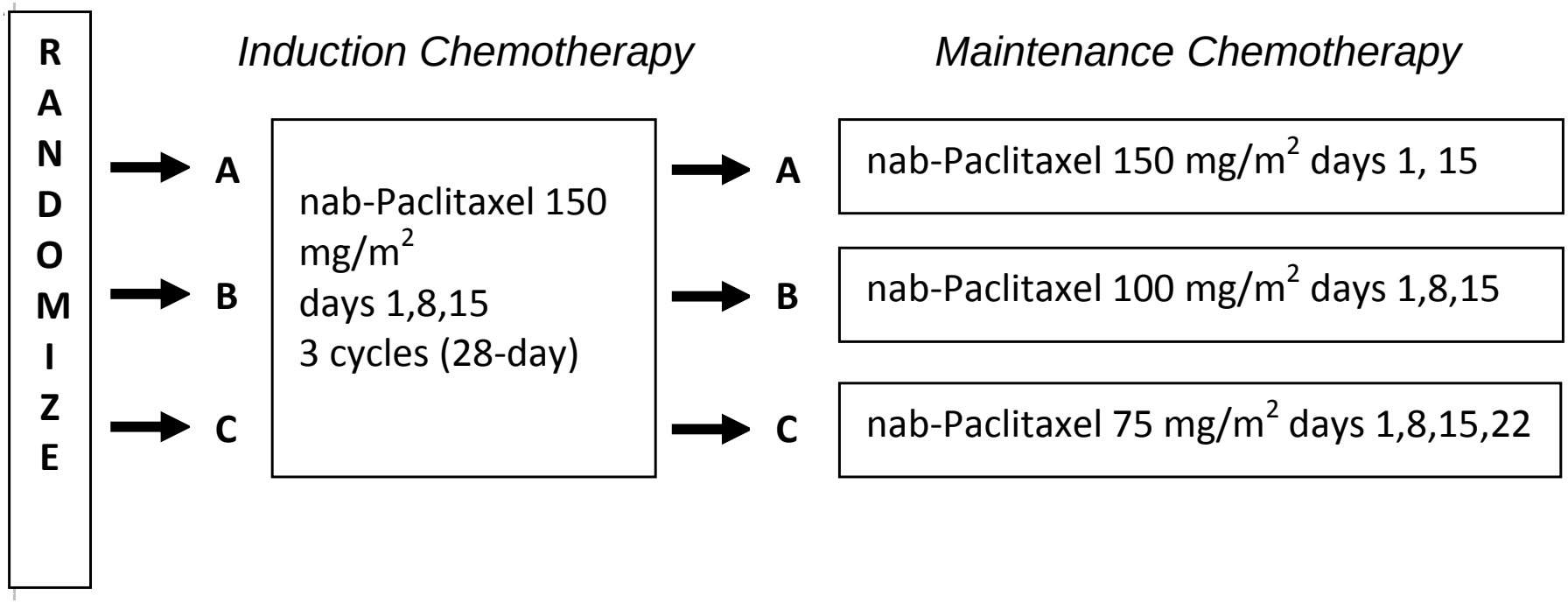
Long Term First-line Chemotherapy
Alternative Schedules: Dose Density Hypothesis



SNAP Design

First line chemotherapy for metastatic breast cancer



In case of toxicity, frequent dose-delays and treatment discontinuation should be avoided

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SNAP Accrual and Study Duration

- Target Accrual: 240 patients
  - (Arm A: 80, Arm B: 80, Arm C: 80)
  - 88% power if median PFS of any arm is at least 10 mos. compared with reference 7 mos.
- Study Duration
  - Randomization during 30 months
  - Additional 12 months of follow-up after the last patient entered
- BIG Supporter Trial: IBCSG (coordinating)

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SNAP Amendment 1

- In the original design, during induction phase, 3 cycles of nab-Paclitaxel 150 mg/m^2 days 1, 8, 15 every 28 days.
- First safety review (conducted in March 2014) on 48 patients:
  - Few patients completed the three cycles of induction regimen without dose modification.
  - The median of actually administered doses corresponds to a dose level of about 125 mg/m^2 given 3 out of 4 weeks.
- In Amendment 1 (activated 5 September 2014), the dose in the induction phase was modified to 125 mg/m^2 days 1, 8, 15 every 28 days.
- Approximately 123 patients were treated with 150 mg/m^2 as starting dose during induction.

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Patient Characteristics

	nab-P Maintenance Dose		
	150 mg/m^2 (n = 83)	100 mg/m^2 (n = 86)	75 mg/m^2 (n = 86)
Age, median, years	58	55.5	60
Age > 70 years, %	11	14	16
ECOG PS 0, %	59	69	63
ER positive, %	87	80	80
Measurable disease, %	82	85	80
Visceral disease, %	64	77	76
Number of metastatic sites ≤ 3, %	89	83	81
Prior adjuvant chemotherapy, %	53	62	48
Prior taxanes, %	31	33	30
Prior endocrine therapy for MBC, %	36	35	38

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Gennari A, et al. Poster at SABCS 2016 [abstract P5-15-05].

Adverse Events Induction Therapy

AE, %[a]	*nab*-P 150 mg/m^2 n = 122				*nab*-P 125 mg/m^2 n = 133		
Max AE grade	**2**	**3**	**4**	**5**	**2**	**3**	**4**
Peripheral sensory neuropathy	12	3	–	–	8	–	–
Decreased neutrophils	46	21	3	–	20	18	5
Decreased platelets	–	–	1	–	–	–	–
Febrile neutropenia	–	2	–	–	–	1	–
Anemia	22	3	–	–	26	2	–
Nausea	7	2	–	–	5	–	–
Vomiting	2	2	–	–	2	1	–
Diarrhea	3	3	–	–	5	4	–
Other grade 3-5 adverse event	–	21	3	2	–	23	3
Patients experiencing ≥ 1 AE	98				93		

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Adverse Events Maintenance Phase

AE, %[a]	A n = 66 150 Q14			B n = 72 100 d 1,8,15 Q28			C n = 61 75 Q8		
Max AE grade	**2**	**3**	**4**	**2**	**3**	**4**	**2**	**3**	**4**
Peripheral neuropathy	**29**	**9**	**–**	**31**	**6**	**–**	**25**	**7**	**–**
Decreased neutrophils	15	5	2	24	8	–	21	7	–
Febrile neutropenia	–	–	–	–	1	–	–	–	–
Anemia	9	–	–	18	3	–	10	–	–
Nausea	5	2	–	3	–	–	3	2	–
Vomiting	–	2	–	3	–	–	2	2	–
Diarrhea	–	3	–	3	1	–	7	–	–
Patients' maximum AE grade	40	29	2	44	31	1	28	41	2
Patients experiencing ≥ 1 AE	96			96			97		

[a] Only reporting events grade ≥ 3.

Gennari A, et al. Poster at SABCS 2016 [abstract P5-15-05].

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SNAP Efficacy PFS

Outcome	*nab*-P Maintenance Dose		
	150 mg/m² (n = 83)	100 mg/m² (n = 86)	75 mg/m² (n = 86)
PFS, median (90% CI)	**7.9 (6.8 - 8.4)**	**9.0 (8.1 - 10.9)**	**8.5 (6.7 - 9.5)**
***P* value[a]**	0.12	**0.03**	0.20
Feasibility[b], %	48.2	50.0	51.2
Disease control rates[c], %	65.1	68.6	60.5

- At a median follow-up of 18.2 months, 182 PFS events occurred

[a] Compared with the historical reference PFS. [b] Defined as percentage of patients who completed treatment according to the protocol for at ≥ 24 weeks.
[c] Defined as SD ≥ 24 weeks or PR or CR.

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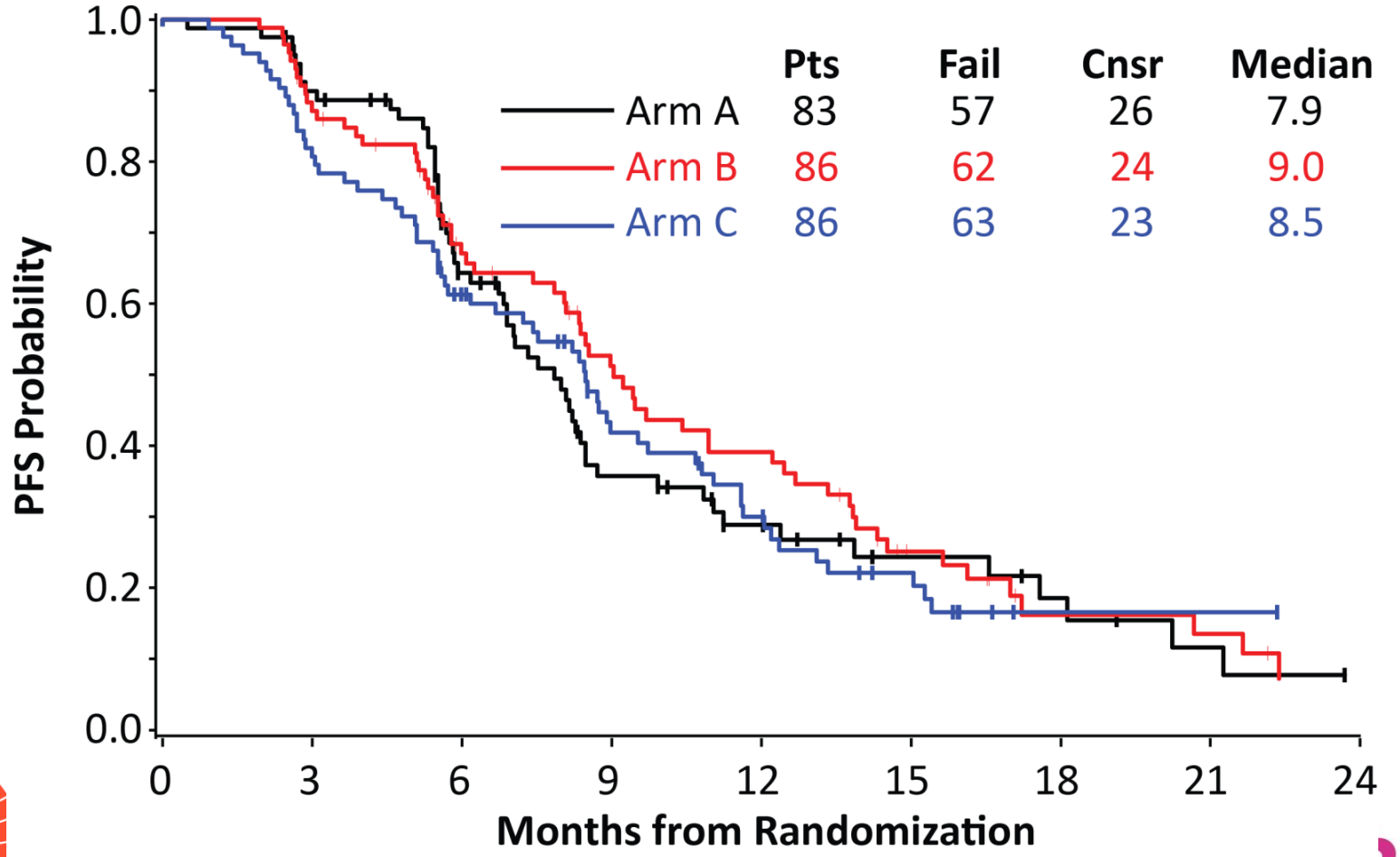
Gennari A, et al. Poster at SABCS 2016 [abstract P5-15-05].

PFS Kaplan Meier



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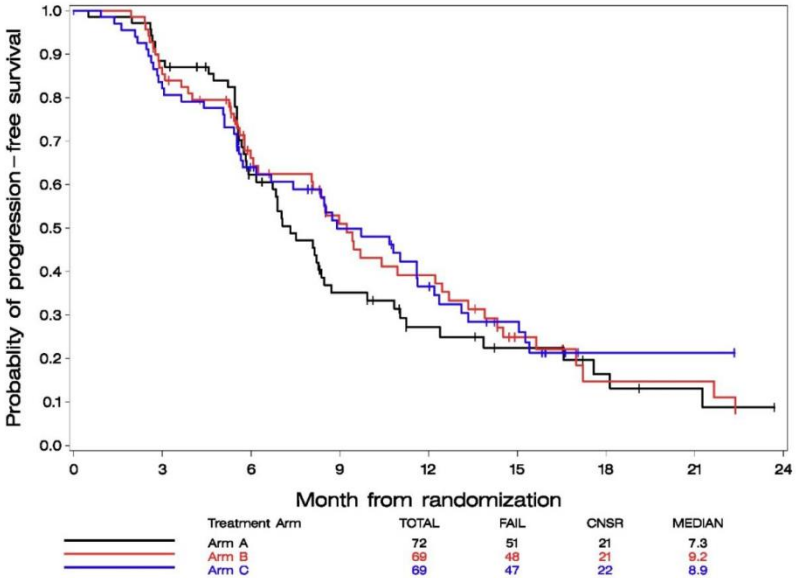
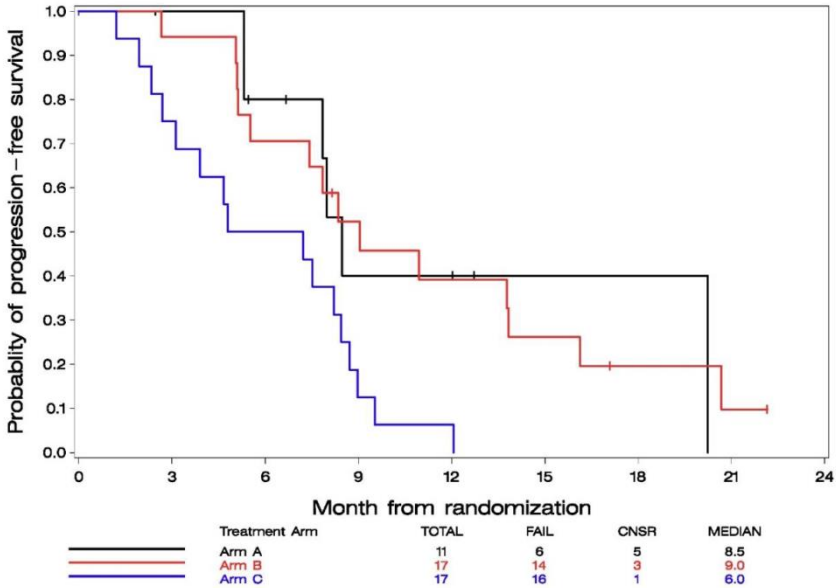
K-M plots of PFS by each treatment arms for ER status

ER positive



ER negative



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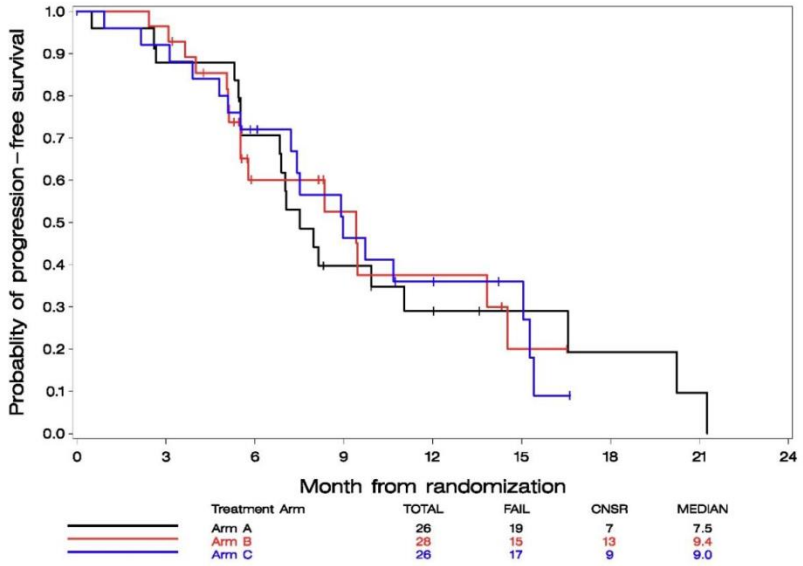
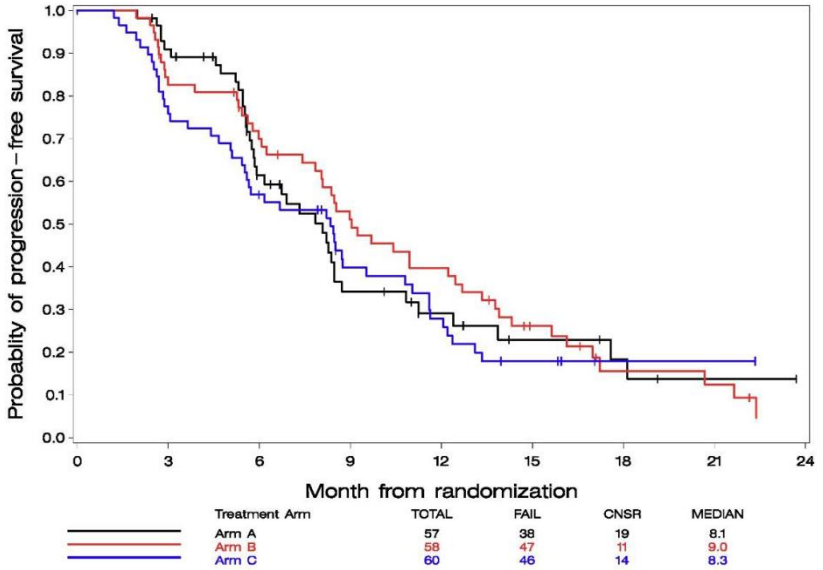
K-M plots of PFS by each treatment arms for prior adjuvant taxanes

Tax yes



Tax no



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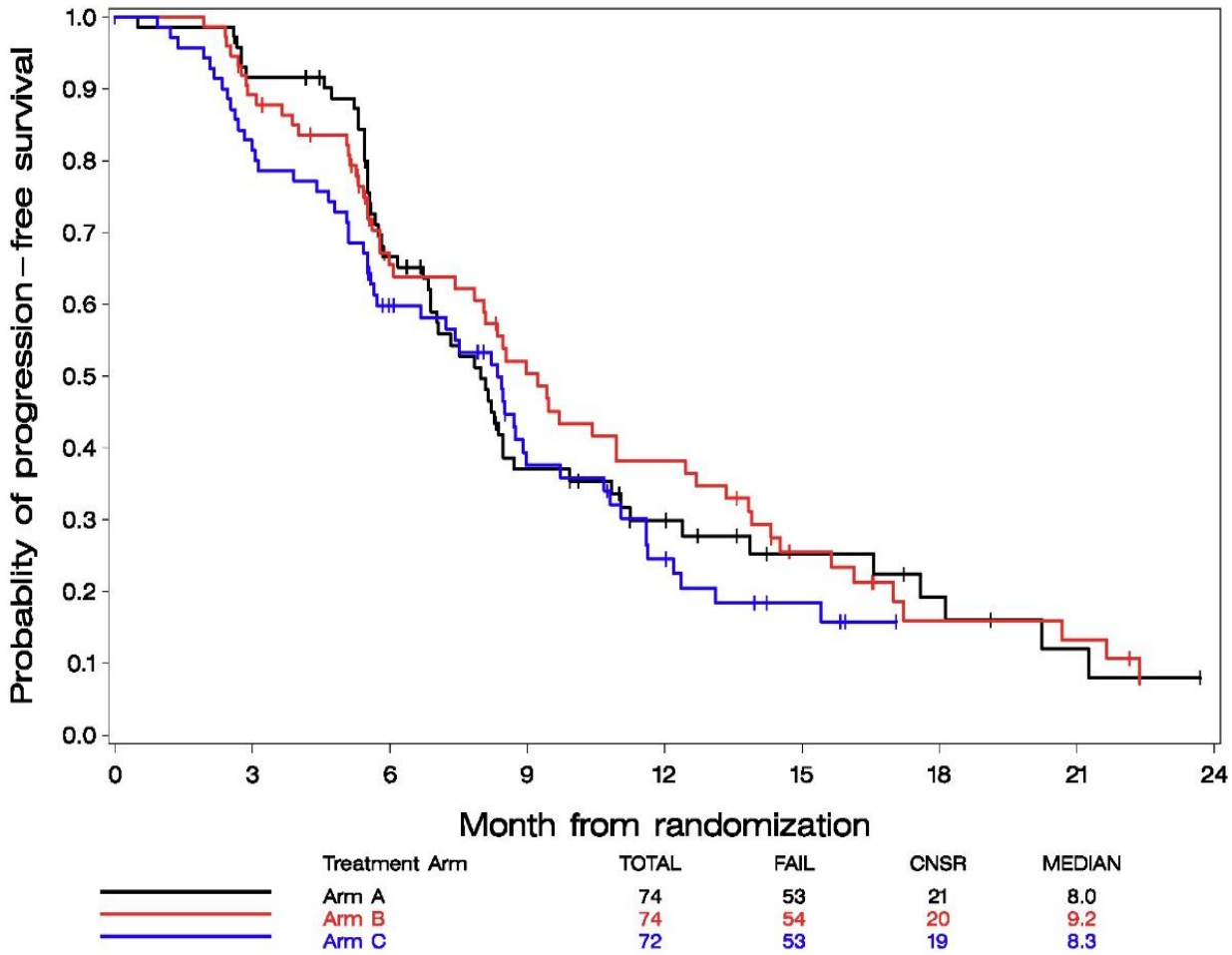
K-M plots of PFS by each treatment arms for patients age <70



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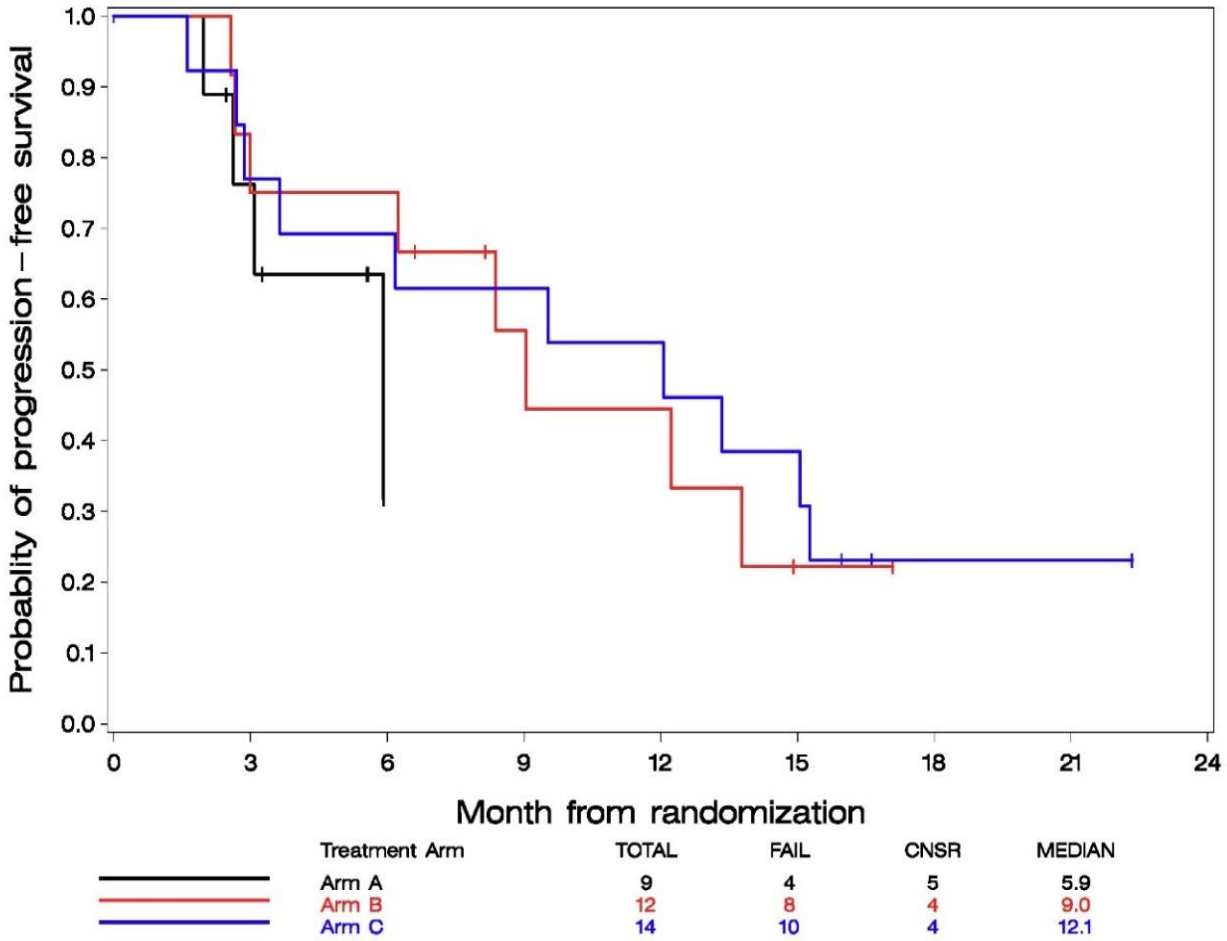
K-M plots of PFS by each treatment arms for patients age ≥ 70



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SNAP Conclusions

- Alternative maintenance CT schedules with reduced doses after a short induction phase at conventional doses are feasible for first line treatment of MBC, and all resulted in a median PFS greater than the historical reference of 7.0 months
- One maintenance schedule, 100 mg/m^2 on days 1, 8, 15[a] (Arm B), had significantly longer median PFS of 9.0 months
- The higher induction dose (150 mg/m^2) was not tolerable
- No new safety signals were observed

[a] Authors' conclusions had "days 1, 8, and 12;" however, the study design had days 1, 8, and 15.

Gennari A, et al. Poster at SABCS 2016 [abstract P5-15-05].

Triple Negative patients

tnAcity
Triple-Negative Albumin-bound paclitaxel Combination International Treatment Study

Annals of oncology 2018

nab-Paclitaxel Plus Carboplatin or Gemcitabine vs Gemcitabine Plus Carboplatin as First-Line Treatment for Patients With Triple-Negative Metastatic Breast Cancer: Results From the tnAcity Trial

DA Yardly,[1] R Coleman,[2] P Conte,[3] J Cortes,[4] A Brufsky,[5] M Shtivelband,[6] R Young,[7] C Bengala,[8] H Ali,[9] J Eakel,[10] A Schneeweiss,[11] L de la Cruz-Merino,[12] S Wilks,[13] J O'Shaughnessy,[14] S Glück,[15] H Li,[16] J Miller[17] D Barton,[17] N Harbeck,[18] on behalf of the tnAcity investigators

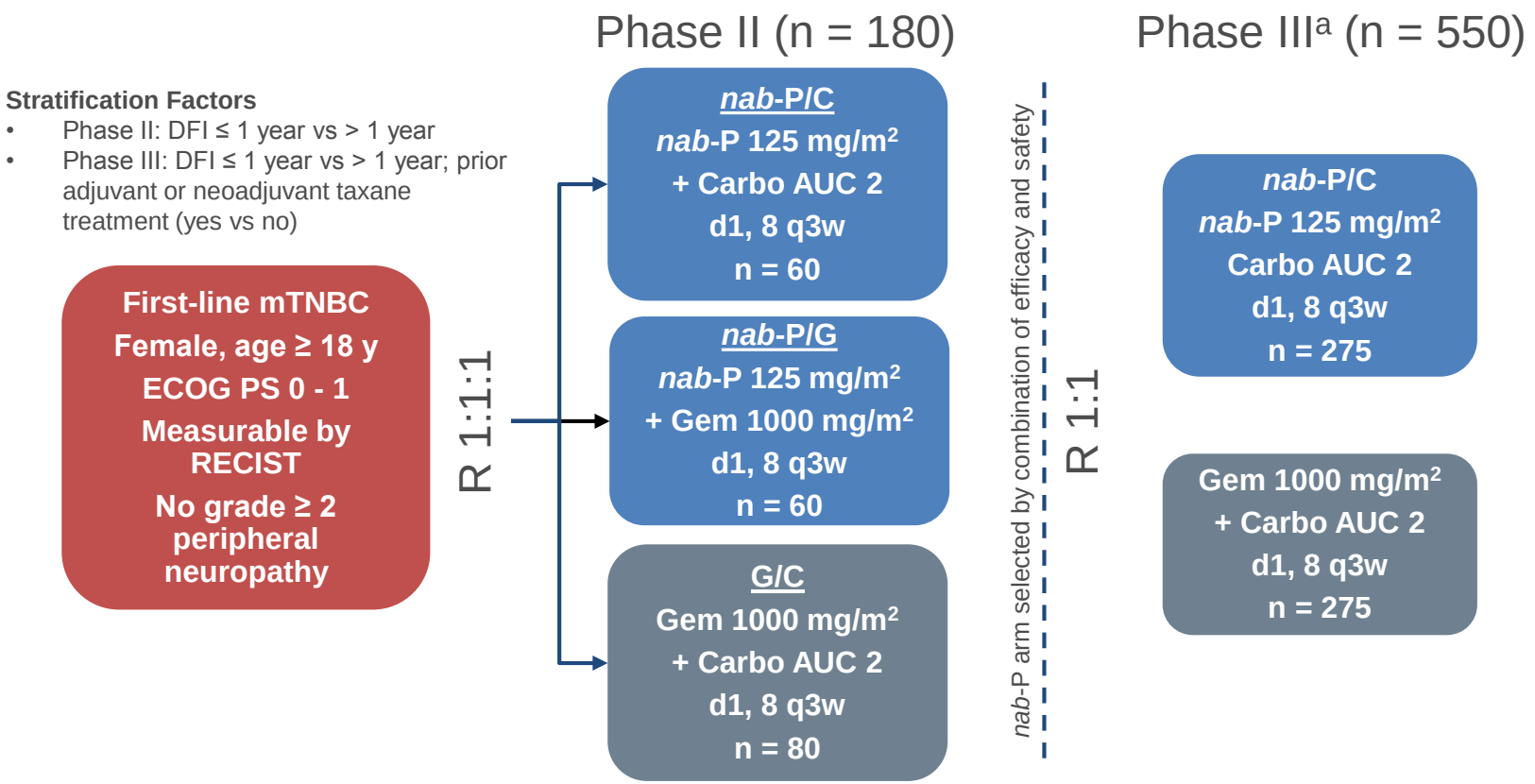
[1]Medical Oncology, Sarah Cannon Research Institute and Tennessee Oncology PLLC, Nashville, TN, USA; [2]Department of Oncology and Metabolism, Weston Park Hospital, University of Sheffield, Sheffield, UK; [3]Department of Surgery, Oncology and Gastroenterology, University of Padova and Medical Oncology 2, Istituto Oncologico Veneto, Padova, Italy; [4]Medical Oncology, Ramon y Cajal University Hospital, Madrid and Vall d'Hebron Institute of Oncology, Barcelona, Spain; [5]Hematology/Oncology, Department of Medicine, University of Pittsburgh School of Medicine, Pittsburgh, PA, USA; [6]Medical Oncology, Ironwood Physicians, PC, Chandler, AZ, USA; [7]Medical Oncology, The Center for Cancer and Blood Disorders, Fort Worth, TX, USA; [8]Medical Oncology, Misericordia General Hospital, Grosseto, Italy; [9]Henry Ford Health System, Detroit, MI, USA; [10]Hematology and Oncology, Florida Cancer Specialists, Sarasota, FL, USA; [11]Gynecology and Medical Oncology, Heidelberg University Hospital, Heidelberg, Germany; [12]Clinical Oncology, Hospital Universitario Virgen Macarena, Seville, Spain; [13]Hematology and Medical Oncology, Texas Oncology, San Antonio, TX, USA; [14]Hematology, Medical Oncology, Baylor Sammons Cancer Center, Texas Oncology, US Oncology, Dallas, TX, USA; [15]GMA Early Assets, Celgene Corporation, Summit, NJ, USA; [16]Department of Biostatistics, Celgene Corporation, Summit, NJ, USA; [17]Clinical Research and Development, Hematology/Oncology, Celgene Corporation, Summit, NJ, USA; [18]Breast Cancer Center, University of Munich, Munich, Germany

tnAcity (ABI-007-MBC-001): Phase II *nab*-P/C, *nab*-P/G or G/C in mTNBC *Objectives*

- Phase II
  - To evaluate efficacy and safety of first-line *nab*-P/C, *nab*-P/G, and G/C in patients with mTNBC
- Only the Phase II results are presented here
- Several novel strategies are being evaluated in phase III TNBC trials including immunotherapy and other treatment modalities[1]
- Successful enrollment of the phase III portion of the tnAcity study, which was designed before the ongoing trials were initiated, was considered unlikely due to these competing trials and a finite existing pool of patients with TNBC; therefore, the phase III portion of the tnAcity trial was canceled

tnAcity (ABI-007-MBC-001): Phase II *nab*-P/C, *nab*-P/G or G/C in mTNBC

schema: phase II and III



- **Primary phase II endpoint:** investigator-assessed PFS
- **Secondary phase II endpoints:** investigator-assessed ORR, percentage of patients who initiated cycle 6 receiving doublet combination therapy, OS, safety

Treatment until disease progression or unacceptable toxicity in both phases

Yardley DA, et al. Ann Oncol. 2018 Jun 6. [Epub ahead of print], by permission of Oxford University Press and the European Society for Medical Oncology.

[a] Patients in phase III are not part of the phase II population.

Yardley DA, Brufsy A, Coleman RE, et al. *nab*-Paclitaxel Plus Carboplatin or Gemcitabine vs Gemcitabine Plus Carboplatin as First-Line Treatment for Patients with Triple-Negative Metastatic Breast Cancer: Results from the tnAcity Trial. *Ann Oncol*. ePub June 6 2018.

tnAcity (ABI-007-MBC-001): Phase II *nab*-P/C, *nab*-P/G or G/C in mTNBC
baseline characteristics (cont)

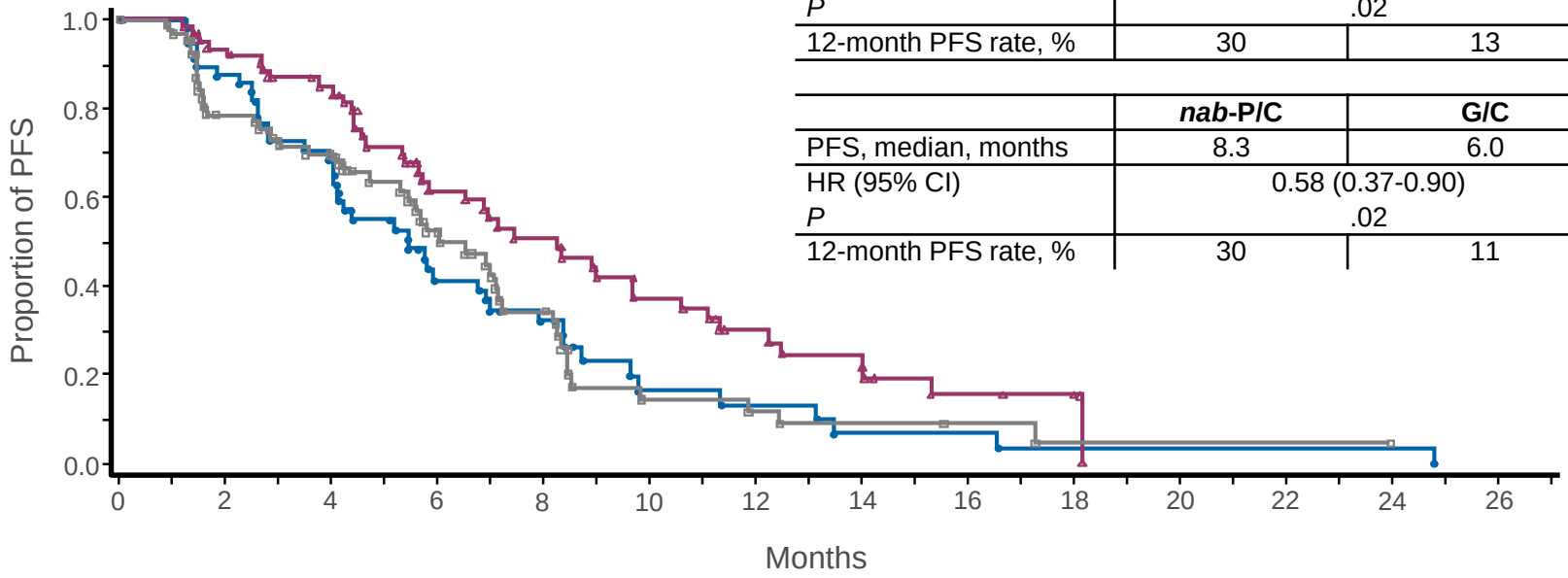
Variable	*nab*-P/C	*nab*-P/G	G/C
	(n = 64)	**(n = 61)**	**(n = 66)**
Disease-free interval, n (%)			
≤ 1 year	16 (25)	17 (28)	20 (30)
> 1 year	48 (75)	43 (70)	45 (68)
Missing	0	1 (2)	1 (2)
Triple negative at primary diagnosis, n (%)	53 (83)	51 (84)	48 (73)
Metastatic triple negative at primary diagnosis, n (%)	17 (27)	11 (18)	10 (15)
Site of metastasis, n (%)			
Lymph node(s)	50 (78)	38 (62)	51 (77)
Lung/thoracic	42 (66)	42 (69)	41 (62)
Bone	21 (33)	23 (38)	25 (38)
Liver	16 (25)	17 (28)	23 (35)
Prior neoadjuvant/adjuvant therapy, n (%)			
Anthracyclines	43 (67)	37 (61)	42 (64)
Taxanes	36 (56)	41 (67)	42 (64)

Yardley DA, Brufsy A, Coleman RE, et al. *nab*-Paclitaxel Plus Carboplatin or Gemcitabine vs Gemcitabine Plus Carboplatin as First-Line Treatment for Patients with Triple-Negative Metastatic Breast Cancer: Results from the tnAcity Trial. ePub June 6 2018.

tnAcity (ABI-007-MBC-001): *progression-free survival*

	***nab*-P/C**	***nab*-P/G**
PFS, median, months	8.3	5.5
HR (95% CI)	0.59 (0.38-0.92)	
P	.02	
12-month PFS rate, %	30	13

	***nab*-P/C**	**G/C**
PFS, median, months	8.3	6.0
HR (95% CI)	0.58 (0.37-0.90)	
P	.02	
12-month PFS rate, %	30	11



Patients at risk

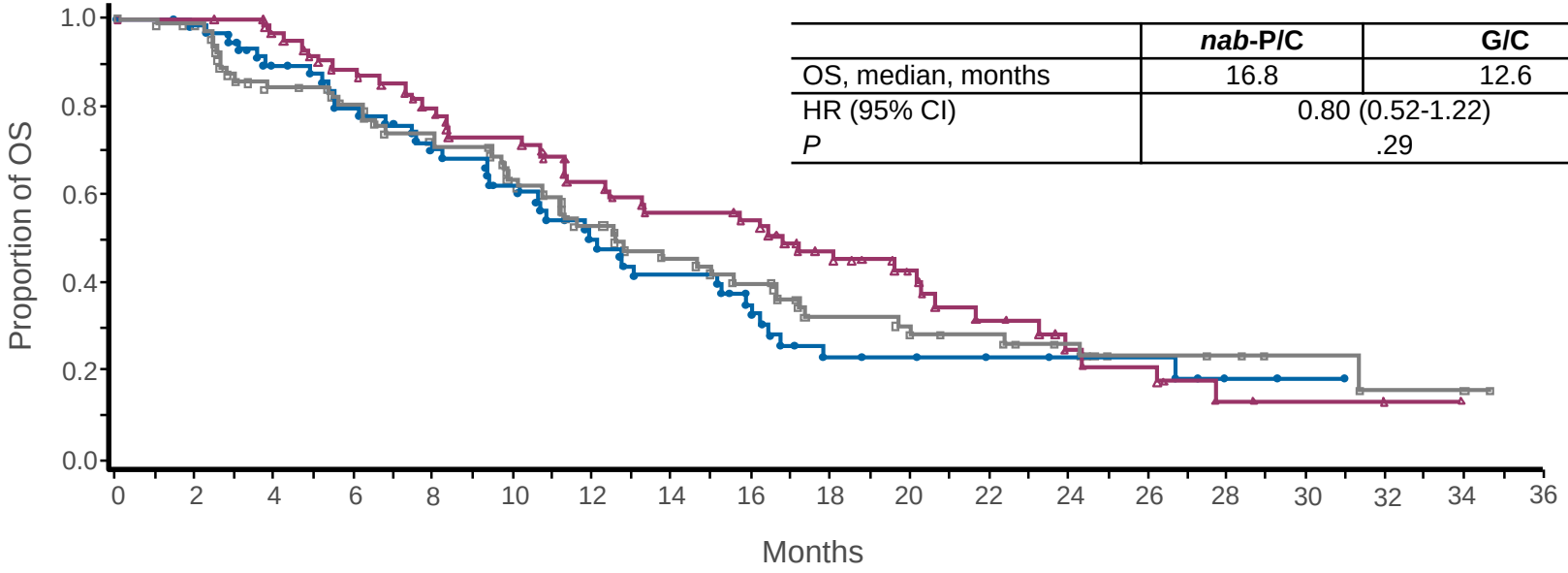
Total:	191	181	150	124	117	92	68	58	49	32	26	25	19	16	14	10	8	6	5	2	2	2	2	2	2	0	0	0
nab-P/C:	64	62	57	49	46	37	29	26	23	19	16	15	11	9	9	5	4	3	3	0	0	0	0	0	0	0	0	0
nab-P/G:	61	57	48	37	35	26	18	15	13	7	5	5	4	4	2	2	2	1	1	1	1	1	1	1	1	0	0	0
G/C:	66	62	45	38	36	29	21	17	13	6	5	5	4	3	3	3	2	2	1	1	1	1	1	1	1	0	0	0

Yardley DA, Brufsy A, Coleman RE, et al. *nab*-Paclitaxel Plus Carboplatin or Gemcitabine vs Gemcitabine Plus Carboplatin as First-Line Treatment for Patients with Triple-Negative Metastatic Breast Cancer: Results from the tnAcity Trial. *Ann Oncol*. ePub June 6 2018.

tnAcity (ABI-007-MBC-001): *overall survival*

	***nab*-P/C**	***nab*-P/G**
OS, median, months	16.8	12.1
HR (95% CI)	0.73 (0.47-1.13)	
P	.16	

	***nab*-P/C**	**G/C**
OS, median, months	16.8	12.6
HR (95% CI)	0.80 (0.52-1.22)	
P	.29	



Patients at risk																																	
Total:	191	189	184	172	160	153	144	134	124	119	110	101	91	82	78	76	68	57	49	44	39	32	30	27	22	17	17	14	10	7	6	5	3	3	1	0	0
nab-P/C:	64	64	64	63	59	56	54	51	47	43	43	40	37	35	33	33	31	27	24	20	17	12	11	10	7	6	6	4	3	2	2	2	1	1	0	0	0
nab-P/G:	61	60	58	55	49	46	42	39	36	35	31	27	24	21	20	20	15	11	9	8	8	7	6	6	5	5	5	4	2	2	1	0	0	0	0	0	0
G/C:	66	65	62	54	52	51	48	44	41	41	36	34	30	26	25	23	22	19	16	16	14	13	13	11	10	6	6	6	5	3	3	3	2	2	1	0	0

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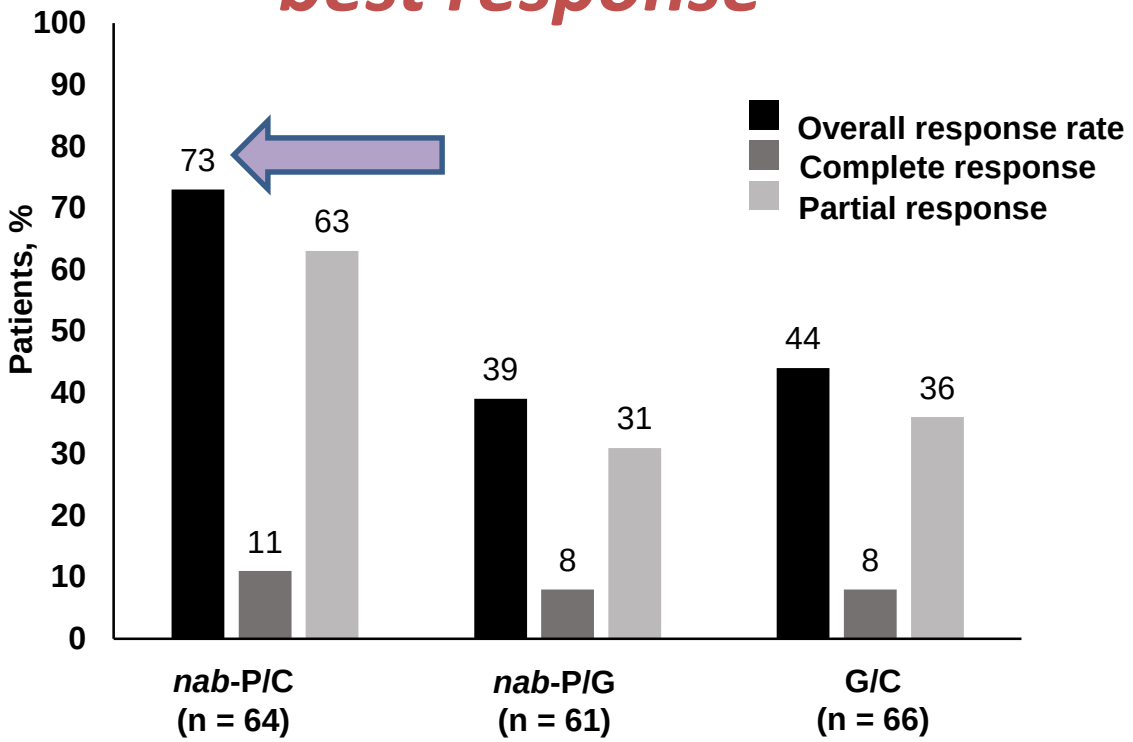
tnAcity (ABI-007-MBC-001): *best response*

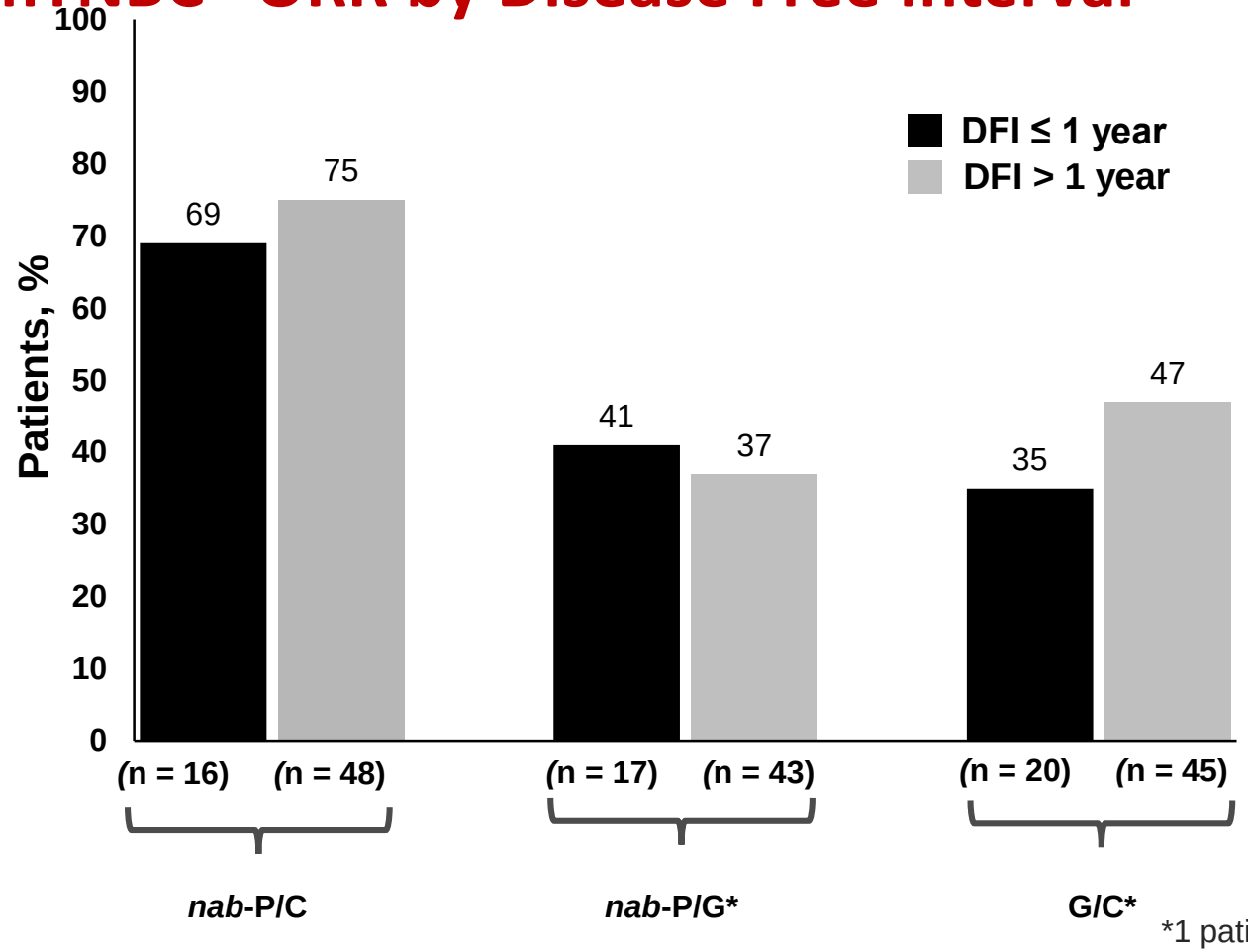


Yardley DA, et al. Ann Oncol. 2018 Jun 6. [Epub ahead of print], by permission of Oxford University Press and the European Society for Medical Oncology.

- The percentage of patients with PD as best response was 6%, 10% and 21% in the *nab*-P/C, *nab*-P/G, and G/C groups, respectively
- mDOR (95% CI) was 6.2 (4.0-10.2) months, 5.8 (2.9-10.4) months, and 5.0 (4.2-7.7) months in the *nab*-P/C, *nab*-P/G, and G/C groups, respectively
- SD of ≥ 16 weeks was achieved by 20%, 44%, and 32% in the *nab*-P/C, *nab*-P/G, and G/C groups, respectively

Yardley DA, Brufsy A, Coleman RE, et al. *nab*-Paclitaxel Plus Carboplatin or Gemcitabine vs Gemcitabine Plus Carboplatin as First-Line Treatment for Patients with Triple-Negative Metastatic Breast Cancer: Results from the tnAcity Trial. *Ann Oncol*. ePub June 6 2018.

tnAcity (ABI-007-MBC-001): Phase II nab-P/C, nab-P/G or G/C in mTNBC ORR by Disease Free Interval



- Overall, 20% of patients had a primary diagnosis of mTNBC and were classified as a DFI > 1 year

Yardley DA, Brufsy A, Coleman RE, et al. *nab*-Paclitaxel Plus Carboplatin or Gemcitabine vs Gemcitabine Plus Carboplatin as First-Line Treatment for Patients with Triple-Negative Metastatic Breast Cancer: Results from the tnAcity Trial. *Ann Oncol*. ePub June 6 2018.

tnAcity (ABI-007-MBC-001): safety (TEAEs)

Parameter, n (%)	*nab*-P/C	*nab*-P/G	G/C
	(n = 64)	(n = 60)	(n = 64)
Patients with TEAE	63 (98)	60 (100)	64 (100)
Grade ≥ 3, total	51 (80)	46 (77)	54 (84)
Grade ≥ 3, hematologic			
Neutropenia	27 (42)	16 (27)	33 (52)
Anemia	8 (13)	7 (12)	17 (27)
Thrombocytopenia	6 (9)	4 (7)	18 (28)
Leukopenia	4 (6)	2 (3)	7 (11)
Febrile Neutropenia	3 (5)	1 (2)	0
Grade ≥ 3, nonhematologic			
Peripheral Neuropathy	3 (5)	4 (7)	1 (2)
Fatigue	2 (3)	9 (15)	2 (3)
Serious	20 (31)	22 (37)	25 (39)
Patients with a TEAE leading to discontinuation of any study drug	29 (45)	16 (27)	15 (23)
Patients with a TEAE leading to dose reduction of any study drug	20 (31)	23 (38)	25 (39)
Patients with a TEAE leading to dose interruption of any study drug	50 (78)	31 (52)	50 (78)
Patients with a TEAE leading to death	1 (2)	2 (3)	2 (3)
Use of growth factors	29 (45)	15 (25)[a]	31 (47)[b]

Yardley DA, et al. Ann Oncol. 2018 Jun 6. [Epub ahead of print], by permission of Oxford University Press and the European Society for Medical Oncology.

tnAcity (ABI-007-MBC-001): Phase II nab-P/C, nab-P/G or G/C in mTNBC

Authors' conclusions

- The results from phase II portion of the tnAcity trial suggest that chemotherapy remains a viable option in patients with mTNBC with manageable toxicity

---

- Treatment with *nab*-P/C resulted in a longer PFS and OS, as well as a higher ORR compared with *nab*-P/G or G/C.
- Treatment with nab-P/C also resulted in a numerically higher ORR in patients with a short DFI

Yardley DA, Brufsy A, Coleman RE, et al. *nab*-Paclitaxel Plus Carboplatin or Gemcitabine vs Gemcitabine Plus Carboplatin as First-Line Treatment for Patients with Triple-Negative Metastatic Breast Cancer: Results from the tnAcity Trial. *Ann Oncol*. ePub June 6 2018.

Nab-paclitaxel

EFFECTIVENESS

(real-world)

IBCSG

BIG
Breast International Group

Drug Design, Development and Therapy

Dovepress
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ORIGINAL RESEARCH

Nanoparticle albumin-bound paclitaxel (nab-paclitaxel) as second-line chemotherapy in HER2-negative, taxane-pretreated metastatic breast cancer patients: prospective evaluation of activity, safety, and quality of life

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Background: A prospective, multicenter trial was undertaken to assess the activity, safety, and quality of life of nanoparticle albumin-bound paclitaxel (nab-paclitaxel) as second-line chemotherapy in HER2-negative, taxane-pretreated metastatic breast cancer (MBC).

Patients and methods: Fifty-two women with HER2-negative MBC who were candidates for second-line chemotherapy for the metastatic disease were enrolled and treated at three centers in Northern Italy. All patients had previously received taxane-based chemotherapy in the adjuvant or first-line metastatic setting. Single-agent nab-paclitaxel was given at the dose of 260 mg/m^2 as a 30-minute intravenous infusion on day 1 each treatment cycle, which lasted 3 weeks, in the outpatient setting. No steroid or antihistamine premedication was provided. Treatment was stopped for documented disease progression, unacceptable toxicity, or patient refusal.

Results: All of the enrolled patients were evaluable for the study endpoints. The objective response rate was 48% (95% CI, 31.5%–61.3%) and included complete responses from 13.5%. Disease stabilization was obtained in 19 patients and lasted >6 months in 15 of them; the overall clinical benefit rate was 77%. The median time to response was 70 days (range 52–86 days). The median progression-free survival time was 8.9 months (95% CI, 8.0–11.6 months, range 5–21+ months). The median overall survival point has not yet been reached. Toxicities were expected and manageable with good patient compliance and preserved quality of life in patients given long-term treatment.

Palumbo *et al.*, 2015

MOVING BEYOND CLINICAL TRIALS: A REAL WORLD MULTICENTER ITALIAN EXPERIENCE WITH ALBUMIN-BOUND PACLITAXEL (*NAB*-PACLITAXEL) IN METASTATIC BREAST CANCER

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STUDY POPULATION

	3qw *Nab*-P 260 mg/m²	qw *Nab*-P 125 mg/m²	OVERALL
No of patients (%)	145	70	215
Median age, years [range]	*52* [31-68]	*55* [45-78]	*54* [31-83]
<65 years	81 (55.9)	29 (41.4)	110 (51.1)
≥65 years	**64 (44.1)**	**41 (58.6)**	**105 (48.8)**
ECOG Performance Status			
0	61 (42.0)	41 (58.5)	102 (47.5)
1	56 (38.6)	16 (22.8)	72 (33.5)
2	28 (19.3)	13 (18.5)	41 (19.0)
Primary tumour subtype (*)			
ER+/PgR+	**58 (40.0)**	**25 (35.7)**	**83 (38.6)**
ER+/PgR-	**37 (25.5)**	**19 (27.1)**	**56 (26.0)**
ER-/PgR+	**14 (9.6)**	**8 (11.4)**	**22 (10.2)**
ER-/PgR-	36 (24.8)	18 (25.7)	54 (25.1)
Prior systemic therapy (early stage)			
anthracycline-based CT (no taxane)	39 (26.8)	11 (15.7)	50 (23.2)
anthracycline + taxane	57 (39.3)	36 (51.4)	93 (43.2)
taxane only	35 (24.1)	18 (25.7)	53 (24.6)
CMF	14(9.6)	5 (7.1)	19 (8.8)
Median DFI, *months* (range)	*42* (18-98)	*49* (39-141)	*47* (18-141)
≤24 months	62 (42.7)	26 (37.1)	88 (40.9)
>24 months	83 (57.2)	44 (62.8)	127 (59.1)
Prior CT for metastatic disease			
taxane-based	**89 (61.3)**	**50 (71.4)**	**139 (64.6)**
without taxane	56 (38.6)	20 (28.5)	76 (35.3)
Median number of prior CT lines for metastatic disease (range)	*3 (1-5)*	*4 (2-8)*	*3 (1-8)*
1 prior CT line	**78 (53.7)**	**25 (35.7)**	**103 (47.9)**
2 prior CT lines	46 (31.7)	18 (25.7)	64 (29.7)
3 prior CT lines	21 (14.4)	27 (38.5)	48 (22.3)
Visceral involvement	*109 (75.1)*	*35 (50.0)*	*144 (66.9)*
Dominant metastatic sites			
liver	61 (42.0)	20 (28.5)	81 (37.6)
lung	48 (33.1)	15 (21.4)	63 (29.3)
bone/nodes	21 (14.4)	25 (35.7)	46 (21.3)
skin/soft tissues	15 (10.3)	10 (14.2)	25 (11.6)
Number of metastatic sites			
1	38 (26.2)	22 (31.4)	60 (27.9)
2	42 (28.9)	21 (30.0)	63 (29.3)
≥3	65 (44.8)	27 (38.5)	92 (42.7)

(*): c-erbB2 negative

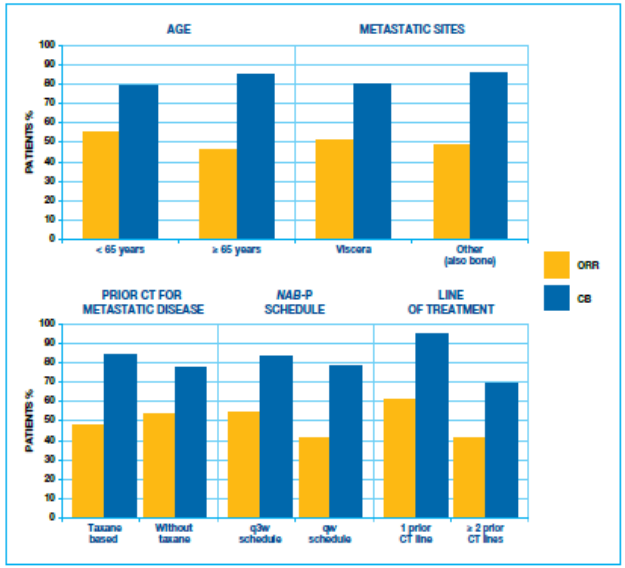
AIMS & METHODS

- To provide a picture of "real life clinical practice" we analyzed the different patterns of treatment and outcome of women receiving single-agent *Nab*-P for their MBC in 9 Centers of Northern Italy from February 2011 to June 2014, with cut-off data evaluation as of December 2014
  - Patients received *Nab*-P as monotherapy intravenously over 30 minutes at the dose of 260 mg/m² every 3 weeks (145 patients) or 125 mg/m² weekly (70 patients) at the discretion of the treating oncologist
  - Treatment was given in the outpatient setting up to disease progression or unacceptable toxicity or patient refusal

TREATMENT ACTIVITY

	3qw *Nab*-P n=145	qw *Nab*-P n=70	OVERALL n=215
Objective RR (%)	79 (54.4)	30 (41.4)	109 (50.6)
Complete response	14 (9.6)	4 (5.7)	18 (8.3)
Partial response	66 (45.5)	25 (35.7)	91 (42.3)
Stable disease ≥16 weeks	41 (28.2)	26 (37.1)	67 (31.1)
Progression disease	24 (16.5)	15 (21.4)	39 (18.1)
Clinical Benefit Rate (CR+PR+SD ≥16 weeks)	121 (83.4)	55 (78.5)	176 (81.8)
Median follow-up	18 months (range 6-36)		
Median PFS in the whole population	7.8 months (range 3.5-23.2+)		
Median PFS in 2nd line subgroup	12.6 months (range 9.2-23.2+)		
Median PFS in ≥3rd line subgroup	4.8 months (range 3.0-5.6)		
Median OS	not yet reached		

SUBGROUP ANALYSIS



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TREATMENT TOXICITY

	3qw *Nab*-P n=145		qw *Nab*-P n=70		OVERALL n=215	
WHO grade	3	4	3	4	3	4
	n (%)		n (%)		n (%)	
Anemia	2 (1.3)	-	-	-	2 (1.3)	-
Leukopenia	25 (17.2)	7 (4.8)	8 (11.4)	-	33 (15.3)	7 (3.2)
Neutropenia	55 (37.9)	27 (18.6)	14 (20.0)	12 (17.1)	69 (32.0)	39 (18.1)
Thrombocytopenia	-	-	-	-	-	-
Diarrhea	4 (2.7)	-	-	-	4 (1.8)	-
Nausea/vomiting	3 (3.5)	-	2 (3.00)	-	5 (2.3)	-
Mucositis	2 (1.3)	-	1 (1.4)	-	3 (1.3)	-
Fatigue	6 (2.7)	-	1 (1.4)	-	7 (3.2)	-
Sensory neuropathy*	27 (18.6)	-	11 (15.7)	-	38 (17.6)	-
Hypersensitivity reactions	-	-	-	-	-	-
Alopecia **	117 (80.6)	-	6 (8.5)	-	123 (57.2)	-

* median time to grade ≤ 2: 19 days (range 14-31) ** grade 1-2 in all patients in the q3w cohort

DURATION OF TREATMENT

	3qw *Nab*-P n=145		qw *Nab*-P n=70		OVERALL n=215	
WHO grade	3	4	3	4	3	4
	n (%)		n (%)		n (%)	
Median no. of cycles (range)	8 (4-27)		5 (3-18)		6 (3-27)	
Required dose reduction (%)	17 (20)		11 (16.9)		28 (18.6)	
Median treatment duration [months (range)]	8 (6-23)		6 (4-15)		6 (4-23)	

KEY POINTS FOR CLINICAL PRACTICE

- **Our "real world" experience, consistent with efficacy published results, confirms that *Nab*-P is a valid chemotherapy option in MBC, also for elderly patients (≥ 65 years)**
- ***Nab*-P could be considered a treatment of choice in MBC for hormone positive receptor and triple negative patients, also taxane-pretreated**
- **Although the well known limitations of a retrospective analysis, these data suggest a better activity of *Nab*-P when administered in early lines**
- **Both 3-weekly and weekly schedules produce encouraging ORR, PFS and CB values, with globally manageable toxicities and good patient compliance in the outpatient setting, in women given long-term treatment too**
- **The median treatment duration was 6 months (4-23): 8 months (6-23) for 3qw schedule and 6 months (4-15) for qw schedule**

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≥3	65 (44.8)	27 (38.5)	92 (42.7)

(*): c-erbB2 negative

→ **48.8% of pts ≥ 65 years**

→ **74.8% of pts hormone-receptor positive**

→ **64.6% of pts taxane pre-treated**

→ **47.9% of pts treated with Nab-P in 2L**

R.Palumbo Presented ESMO 2015

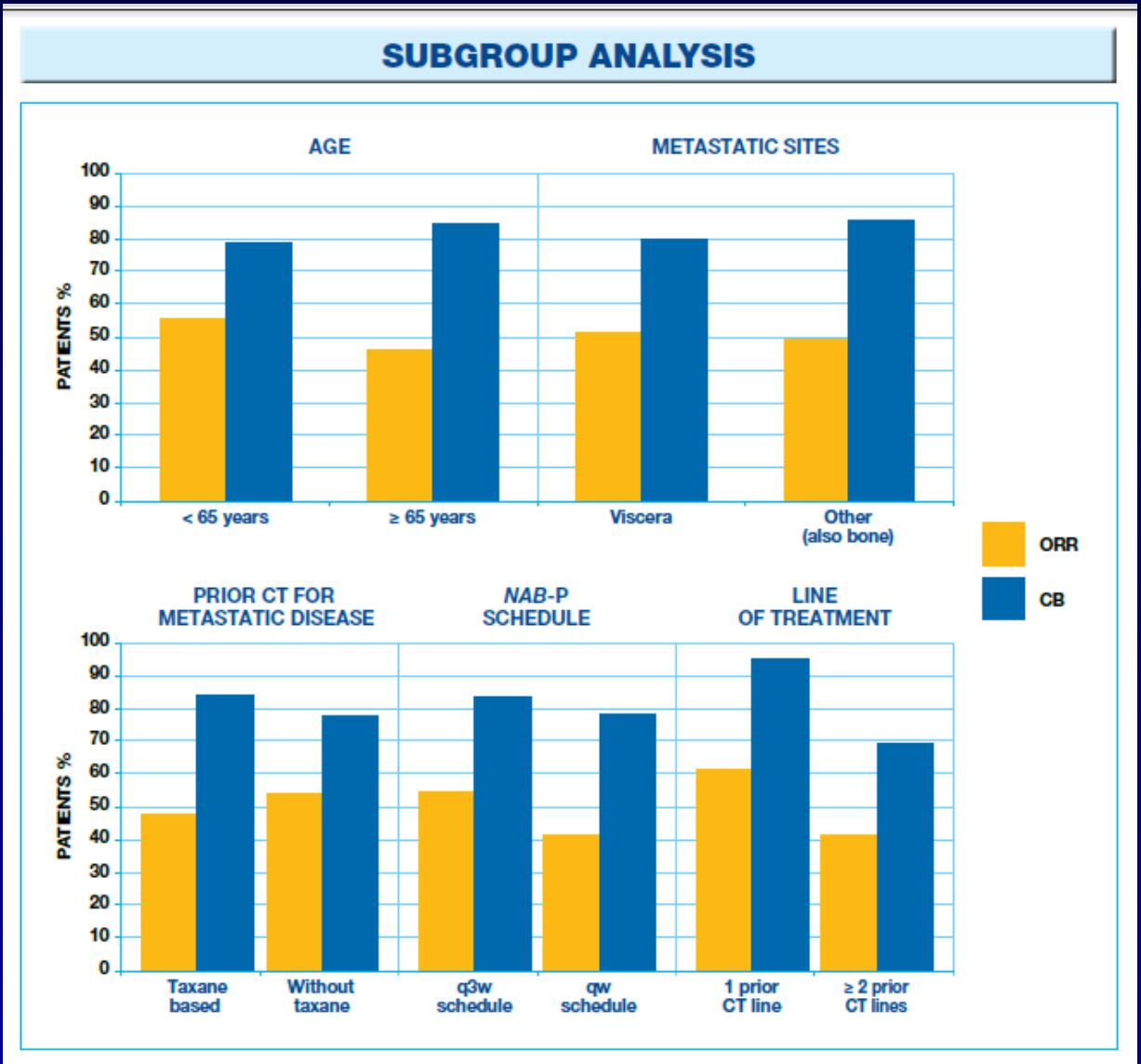
TREATMENT ACTIVITY

	3qw *Nab*-P n=145	qw *Nab*-P n=70	OVERALL n=215
Objective RR (%)	79 (54.4)	30 (41.4)	109 (50.6)
Complete response Partial response Stable disease ≥16 weeks Progression disease	14 (9.6) 66 (45.5) 41 (28.2) 24 (16.5)	4 (5.7) 25 (35.7) 26 (37.1) 15 (21.4)	18 (8.3) 91 (42.3) 67 (31.1) 39 (18.1)
Clinical Benefit Rate (CR+PR+SD ≥16 weeks)	121 (83.4)	55 (78.5)	176 (81.8)
Median follow-up	18 months (range 6-36)		
Median PFS in the whole population	7.8 months (range 3.5-23.2+)		
Median PFS in 2nd line subgroup	12.6 months (range 9.2-23.2+)		
Median PFS in ≥3rd line subgroup	4.8 months (range 3.0-5.6)		
Median OS	not yet reached		

- **Clinical Benefit Rate= 81.8%**
- **Better activity of Nab-p when administered in earlier lines:**

12.6 months of median PFS in 2nd line pts

R.Palumbo Presented ESMO 2015



- **Good activity of Nab-p in terms of ORR and CB in all different pts setting**

R.Palumbo Presented ESMO 2015

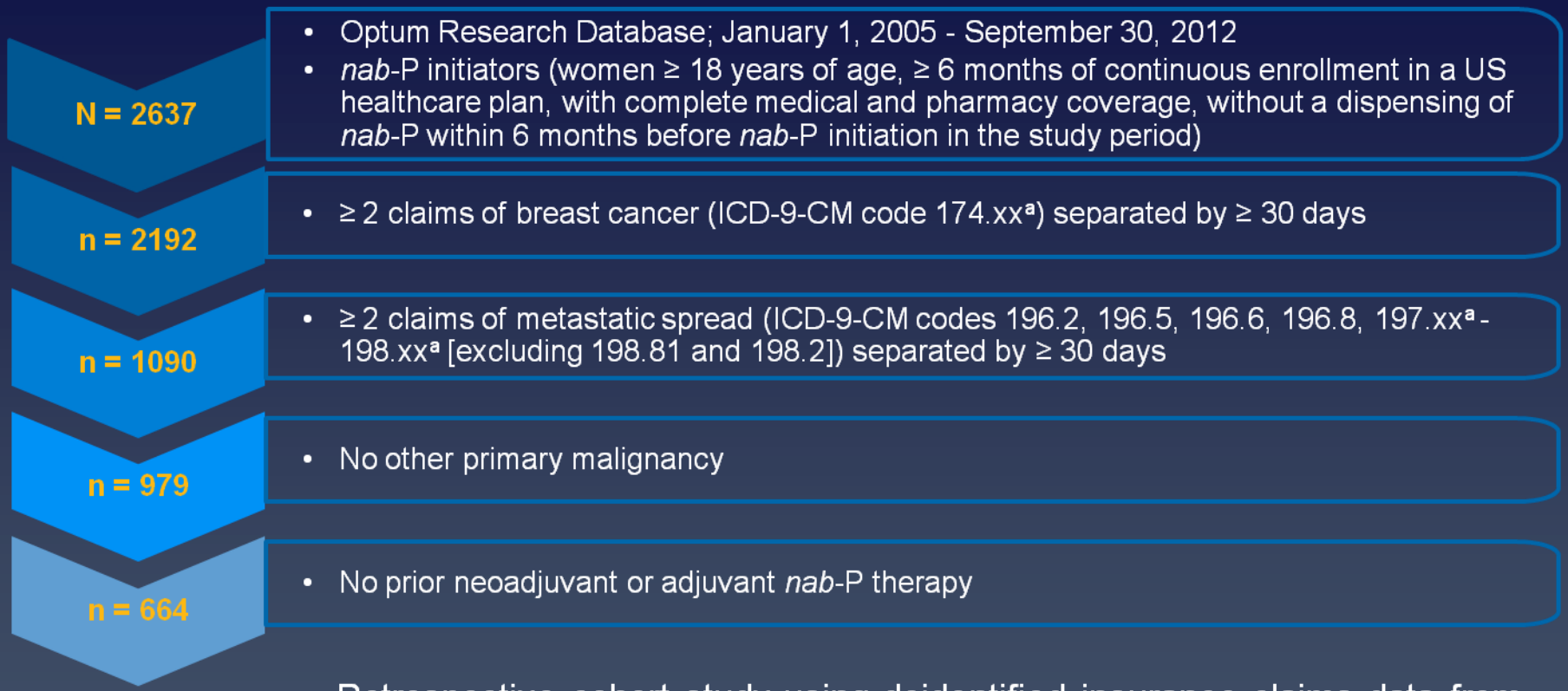
Real-World Efficacy and Safety Outcomes of *nab*-Paclitaxel in Patients With Metastatic Breast Cancer: Results From a US Health Insurance Database

D Patt, C Liang, L Li, A Ko, C Duval Fraser, D Corzo, C Enger

- To characterize the safety and efficacy outcomes of *nab*®-P in patients with MBC in the United States using health insurance claims data

Patt D, Liang C, Li L, et al. Real-world efficacy and safety outcomes of *nab*-paclitaxel in patients with metastatic breast cancer: results from a US health insurance database. Poster presented at: San Antonio Breast Cancer Symposium; December 9 - 13, 2014; San Antonio, TX [poster P3-10-06].

Claims Analysis of nab-P in Patients With MBC
Study Design



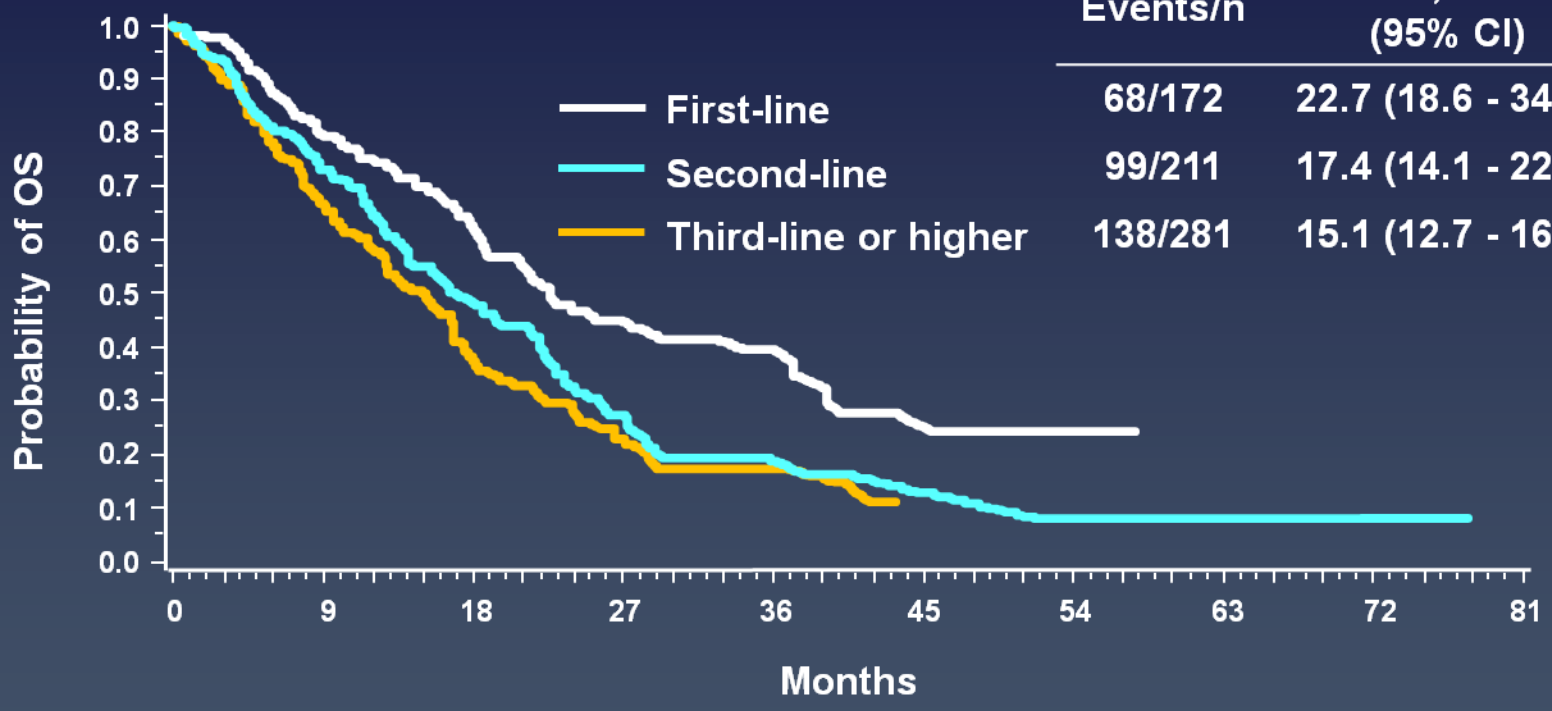
- Retrospective cohort study using deidentified insurance claims data from the Optum Research Database (an affiliate of United Health)
- Data were supplemented by Social Security Death Index sources
- Insured individuals were from geographically diverse US areas

[a] xx indicates any subcode.

ICD-9-CM, International Classification of Diseases, 9th revision, Clinical Modification; MBC, metastatic breast cancer; *nab*-P, *nab*-paclitaxel.

Patt D, Liang C, Li L, et al. Real-world efficacy and safety outcomes of *nab*-paclitaxel in patients with metastatic breast cancer: results from a US health insurance database. Poster presented at: San Antonio Breast Cancer Symposium; December 9 - 13, 2014; San Antonio, TX [poster P3-10-06].

Claims Analysis of *nab*-P in Patients With MBC
Efficacy: OS by Line of Therapy



	Events/n	Median, months (95% CI)
First-line	68/172	22.7 (18.6 - 34.3)
Second-line	99/211	17.4 (14.1 - 22.3)
Third-line or higher	138/281	15.1 (12.7 - 16.9)

MBC, metastatic breast cancer; *nab*-P, *nab*-paclitaxel; OS, overall survival.

Patt D, Liang C, Li L, et al. Real-world efficacy and safety outcomes of *nab*-paclitaxel in patients with metastatic breast cancer: results from a US health insurance database. Poster presented at: San Antonio Breast Cancer Symposium; December 9 - 13, 2014; San Antonio, TX [poster P3-10-06].

Illness trajectory in MBC