Patientinnentag 2019 AGAPLESION MARKUS KRANKENHAUS

Welche Daten sind für Sie aus dem letzten Jahr relevant?

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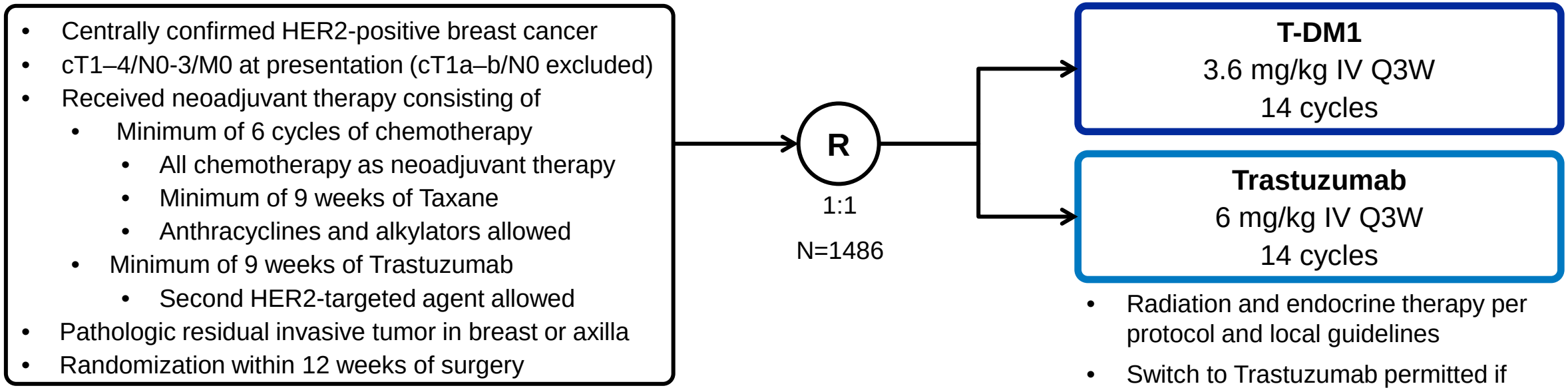
KATHERINE (Phase III) – Study Design

T-DM1 vs. Trastuzumab (postneo-)adjuvant beim HER2+ Mammakarzinom und invasivem Tumorrest nach neoadjuvanter Chemotherapie



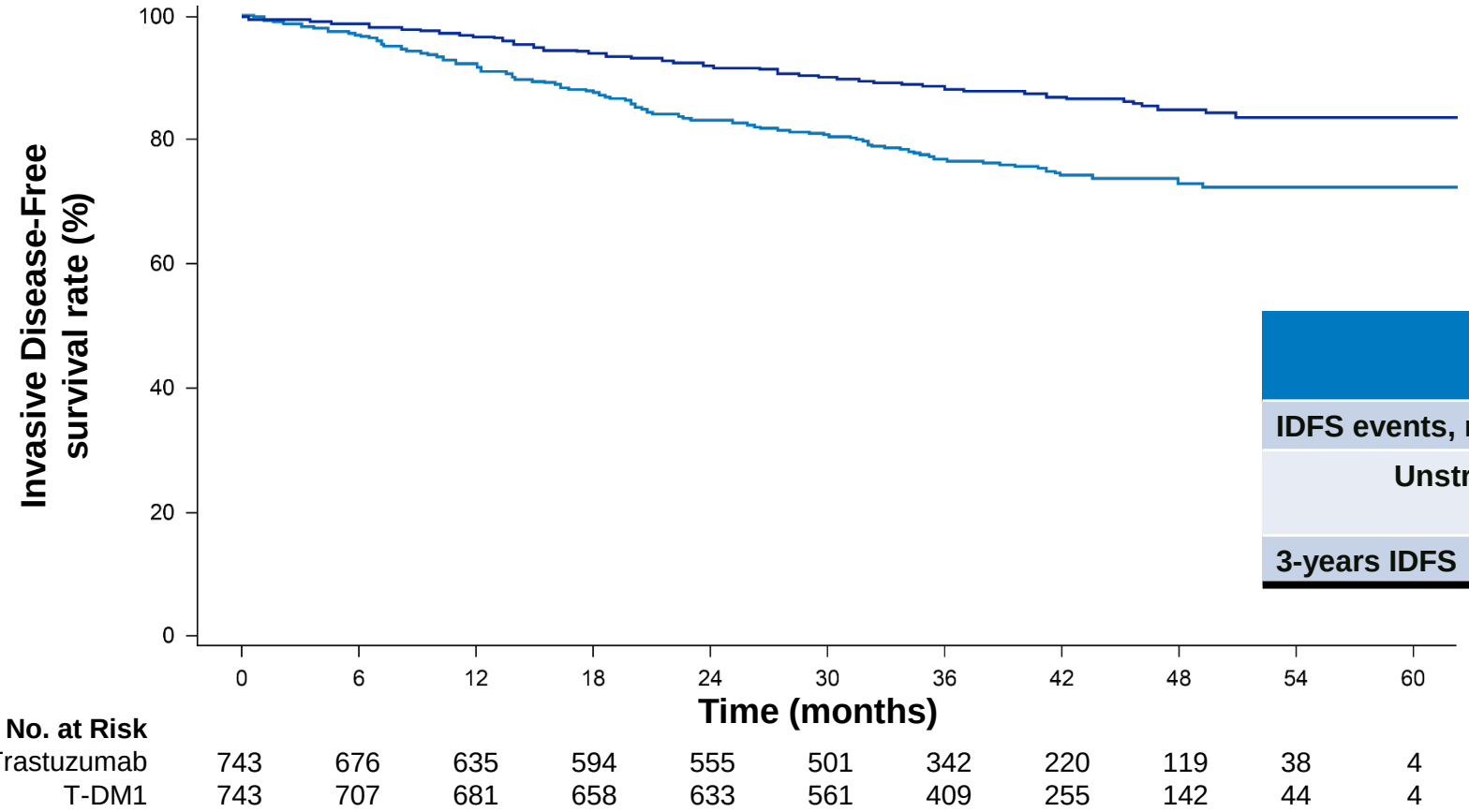
Stratification factors:

- Clinical presentation: Inoperable (stage cT4 or cN2–3) vs. operable (stages cT1–3N0–1)
- Hormone receptor: ER or PR positive vs. ER negative and PR negative/unknown
- Preoperative therapy: Trastuzumab vs. Trastuzumab plus other HER2-targeted therapy
- Pathological nodal status after neoadjuvant therapy: Positive vs. negative/not done

Mod. Geyer CE et al. SABCS 2018, Oral Session – General Session 1, Abstract No. GS1-10

KATHERINE (Phase III) – IDFS (Primary Endpoint)

T-DM1 vs. Trastuzumab (postneo-)adjuvant beim HER2+ Mammakarzinom und invasivem Tumorrest nach neoadjuvanter Chemotherapie



	Trastuzumab (n=743)	T-DM1 (n=743)
IDFS events, no. (%)	165 (22.2)	91 (12.2)
Unstratified HR=0.50 (95% CI, 0.39–0.64) p<0.0001		
3-years IDFS	77.0%	88.3%

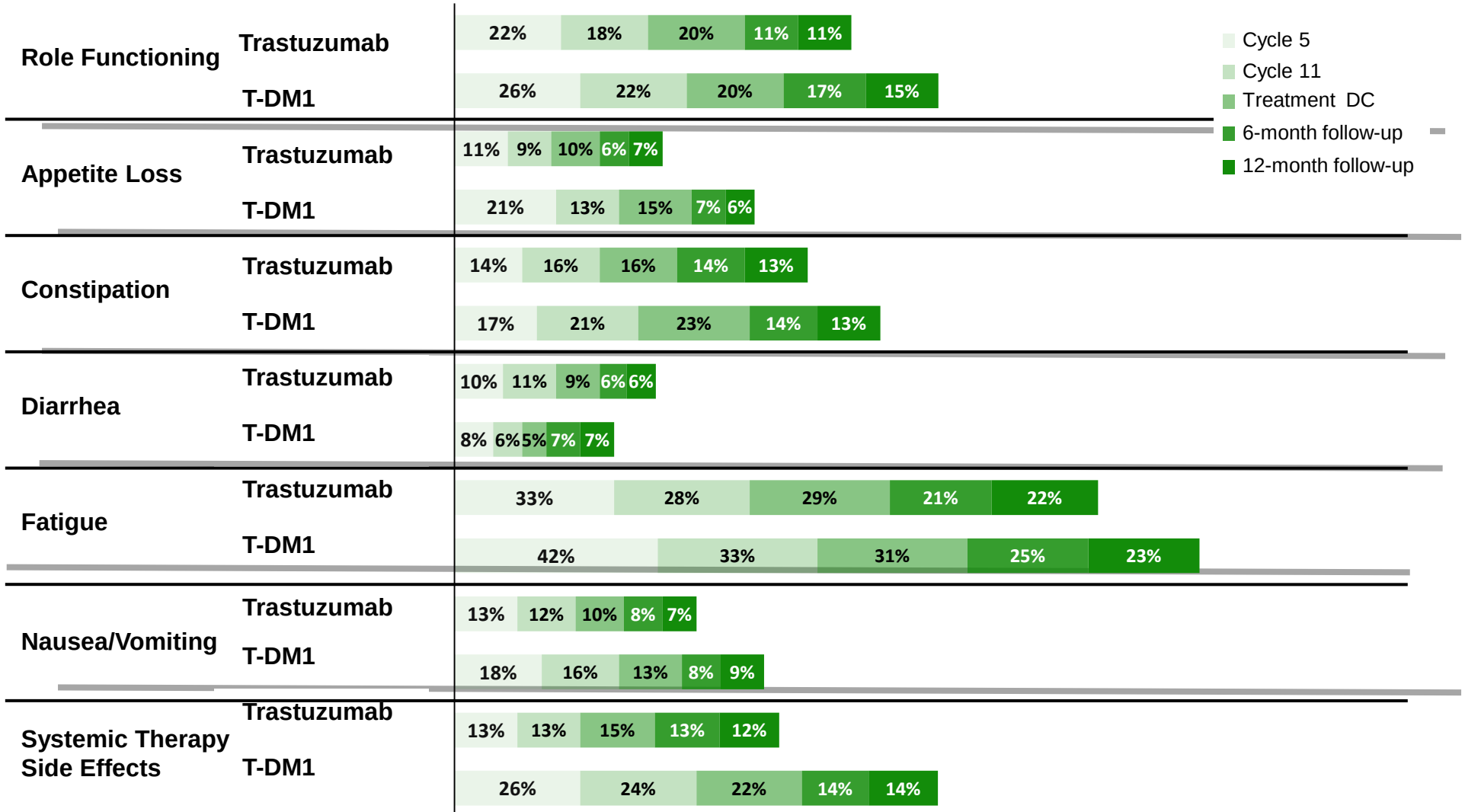
Mod. Geyer CE et al. SABCS 2018, Oral Session – General Session 1, Abstract No. GS1-10

Patient-reported outcomes from KATHERINE: a phase III study of adjuvant trastuzumab emtansine (T-DM1) vs trastuzumab in patients with residual invasive disease after neoadjuvant therapy for HER2-positive breast cancer

Schneeweiss A et al. Poster Session – Breast Cancer – Local/Regional/Adjuvant
Abstract No. 513

KATHERINE – PRO Results: Clinically Meaningful Deterioration at ANY Assessment

- There were small differences in frequency of clinically meaningful deterioration between treatment arms at some time points. However these generally did not persist and were no longer apparent at the 6 month follow-up



Mod. Schneeweiss A et al. ASCO 2019, Poster Session – Breast Cancer – Local/Regional/Adjuvant, Abstract No. 513

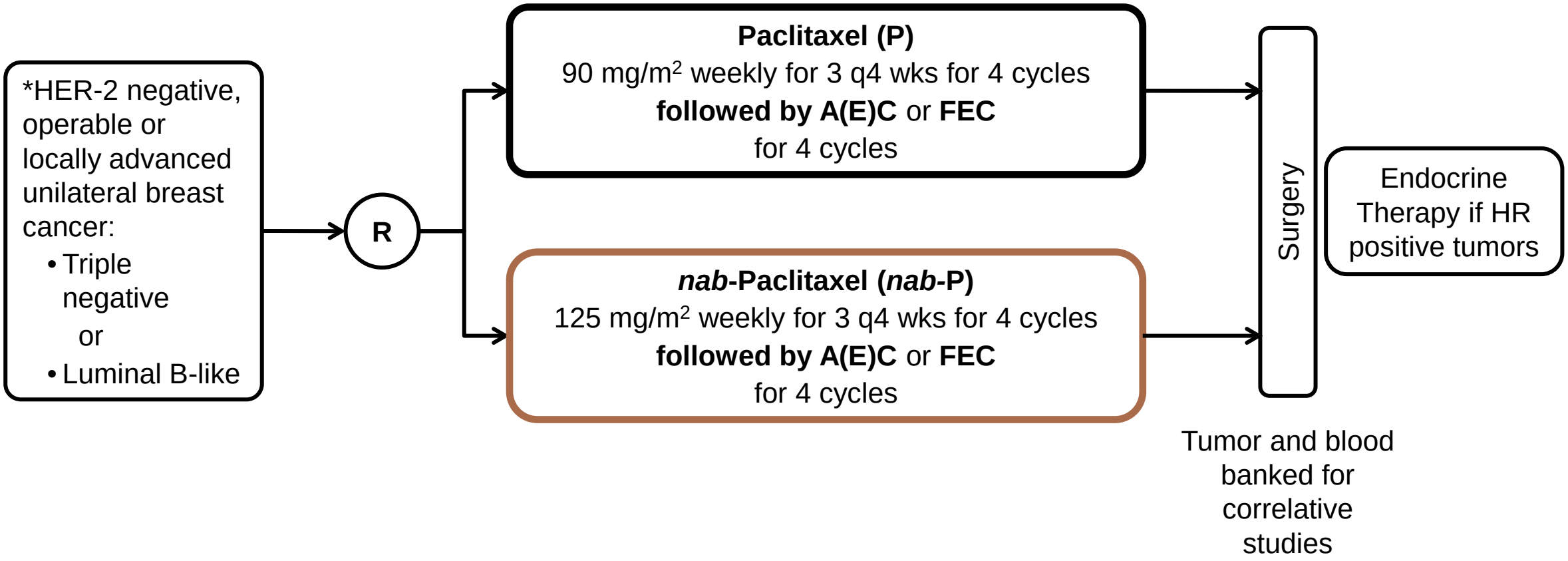
Event-free survival analysis of the prospectively randomized phase III ETNA study with neoadjuvant nab-paclitaxel (*nab*-P) versus paclitaxel (P) both followed by anthracycline regimens in women with HER2-negative high-risk breast cancer. A Michelangelo study in collaboration with GECAM and BCRC-WA

Gianni L et al. Poster Session – Breast Cancer – Local/Regional/Adjuvant

Abstract No. 515

ETNA (Phase III) – Study Design

nab-Paclitaxel vs. Pac → A(E)C/FEC als neoadj. CT beim HER2– EBC (N=695)

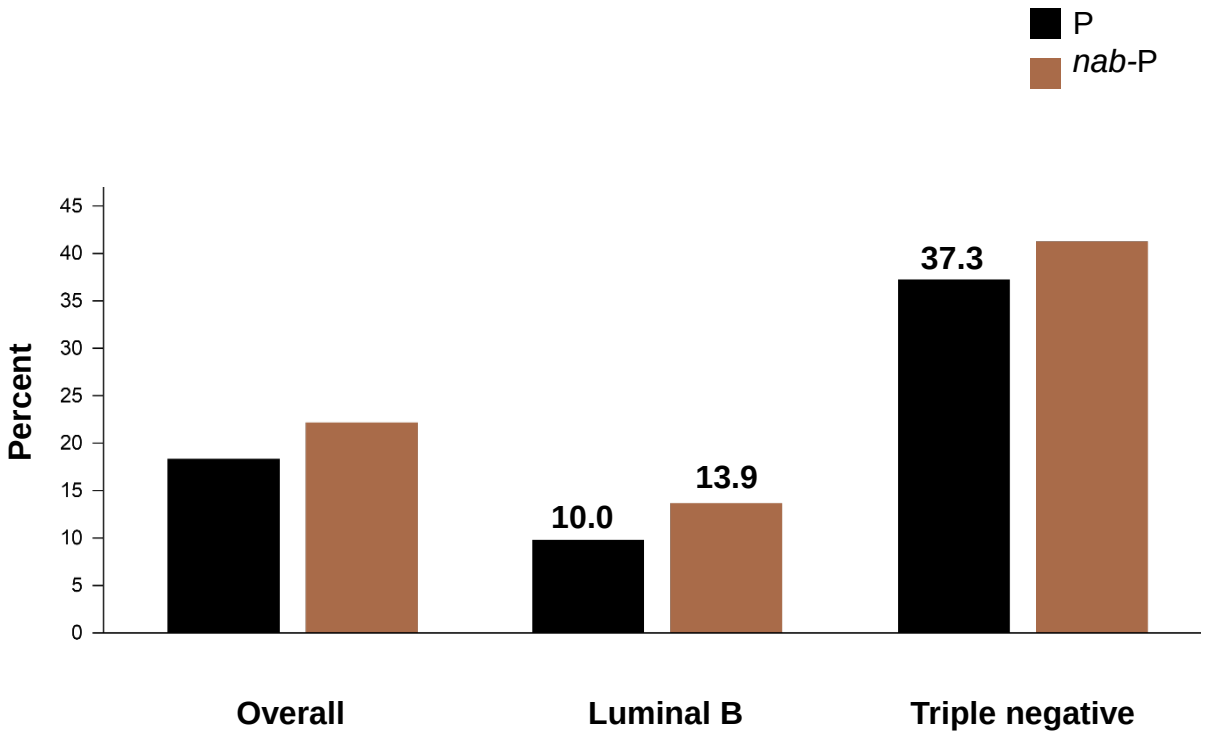


*Estrogen receptor, progesterone receptor, HER2 and Ki67 were centrally assessed before randomization

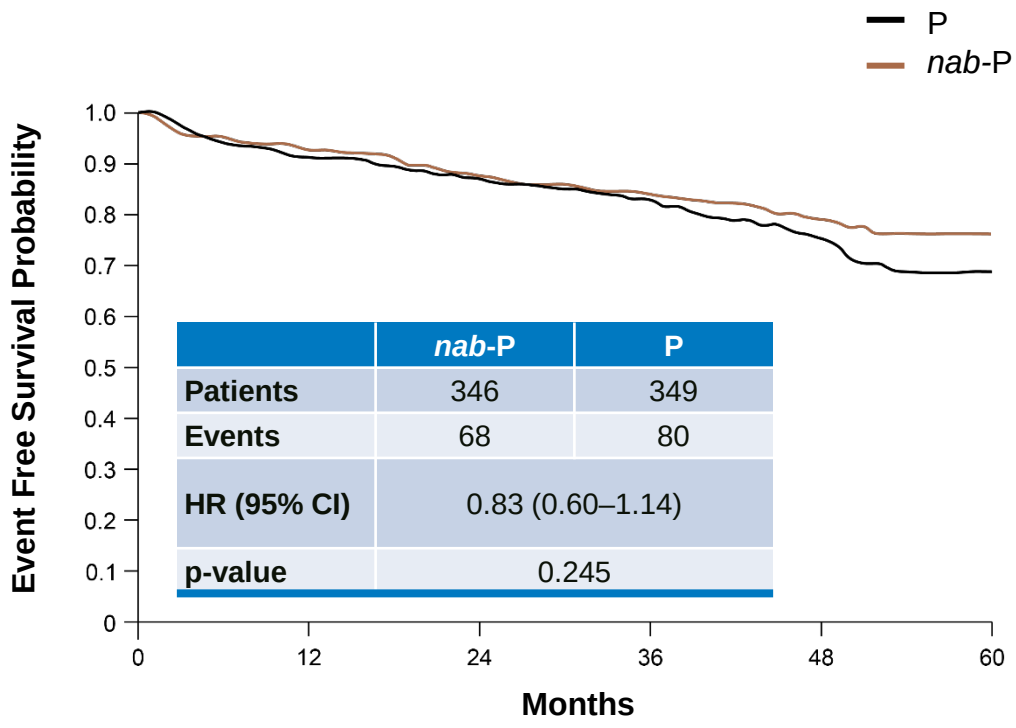
Mod. Gianni L et al. ASCO 2019, Poster Session – Breast Cancer – Local/Regional/Adjuvant, Abstract No. 515

ETNA (Phase III) – pCR, EFS

nab-Paclitaxel vs. Pac → A(E)C/FEC als neoadj. CT beim HER2– EBC (N=695)



Overall: P vs. *nab*-P –3.9 (–9.9–2.1); Odds ratio: 0.77 (0.52–1.13); p value 0.186



	nab-P	P
Patients	346	349
Events	68	80
HR (95% CI)	0.83 (0.60–1.14)	
p-value	0.245	

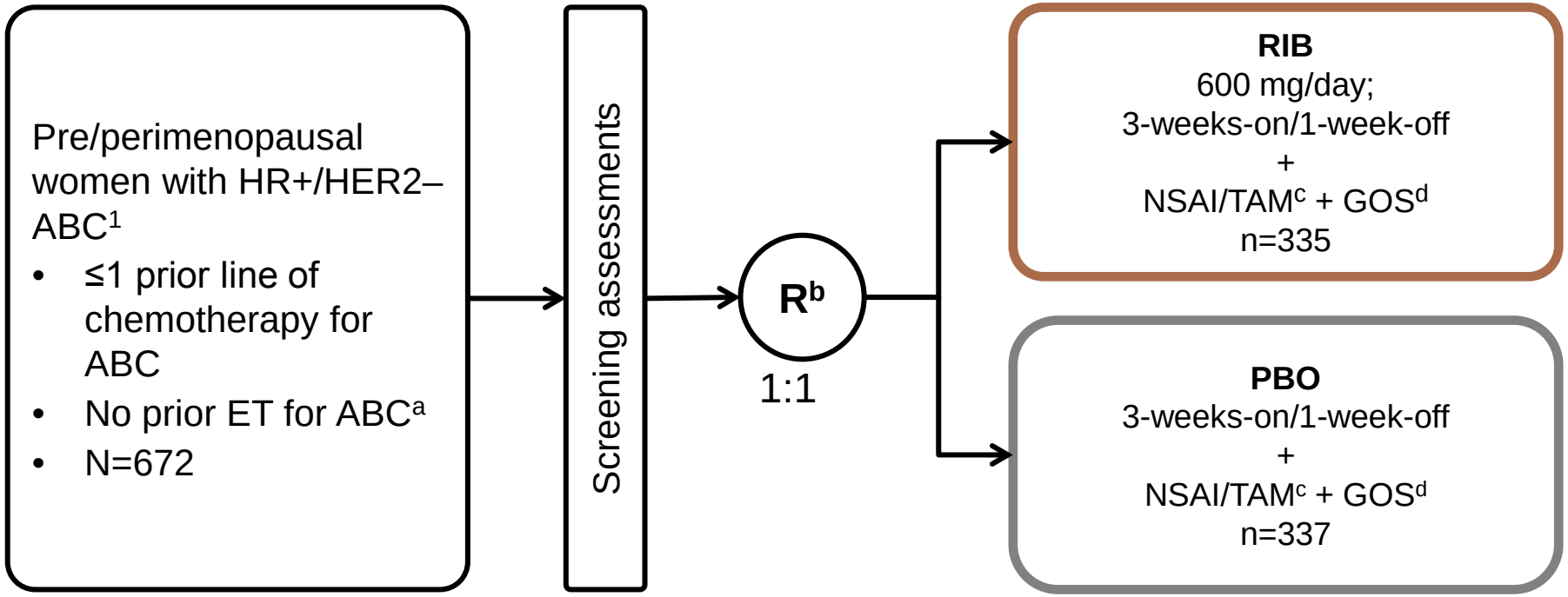
Mod. Gianni L et al. ASCO 2019, Poster Session – Breast Cancer – Local/Regional/Adjuvant, Abstract No. 515

Phase III *MONALEESA-7 Trial* of Premenopausal Patients With HR+/HER2– Advanced Breast Cancer Treated With Endocrine Therapy ± Ribociclib: Overall Survival Results

Hurvitz SA et al. Oral Abstract Session – Breast Cancer – Metastatic

Abstract No. LBA1008

MONALEESA-7 – Study Design



Primary end point
- PFS (local)

Selected secondary end points
- HRQoL
- OS
- ORR
- TTDD of ECOG PS
- Safety

1. Tripathy D et al. *Lancet Oncol*. 2018;19:904-915.
[a]Patients who received ≤14 days of NSAI/TAM ± GOS were allowed. [b]Stratified by liver/lung metastasis (yes/no), prior chemotherapy (yes/no), and combination partner (NSAI/TAM). [c]TAM or NSAI were administered daily orally. TAM dose was 20 mg, LET dose was 2.5 mg, ANA dose was 1 mg. [d]GOS 3.6 mg was administered by subcutaneous injection.
ANA, Anastrozole; ECOG PS, Eastern Cooperative Oncology Group performance status; HRQoL, health-related quality of life; LET, Letrozole; ORR, objective response rate; OS, overall survival; TTDD, time to definitive deterioration.

MONALEESA-7 – Results

Signifikant längeres OS mit RIB + ET vs. PBO + ET

- Median follow-up 34.6 mo (min 28.0 mo); OS was evaluated after 192 deaths (RIB: n=83; PBO: n=109)
- Significantly longer OS with RIB + ET vs. PBO + ET (median not reached vs. 40.9 mo; 95% CI 37.80 mo-not evaluable; HR 0.712; 95% CI 0.54–0.95; p=0.00973). The result crossed the prespecified stopping boundary for superior efficacy
- Estimated OS rates at 42 mo: 70.2% vs. 46.0%
- In pts who received an NSAI (n=495), RIB + ET demonstrated a consistent OS improvement vs. PBO + ET (HR 0.699; 95% CI 0.50–0.98)
- Posttreatment therapy use was balanced between treatment arms (RIB: 68.9%; PBO: 73.2%)
- At cutoff, 173 pts were continuing study treatment (RIB, n=116; PBO, n=57)

Mod. Hurvitz SA et al. ASCO 2019, Oral Abstract Session – Breast Cancer – Metastatic, Abstract No. LBA1008

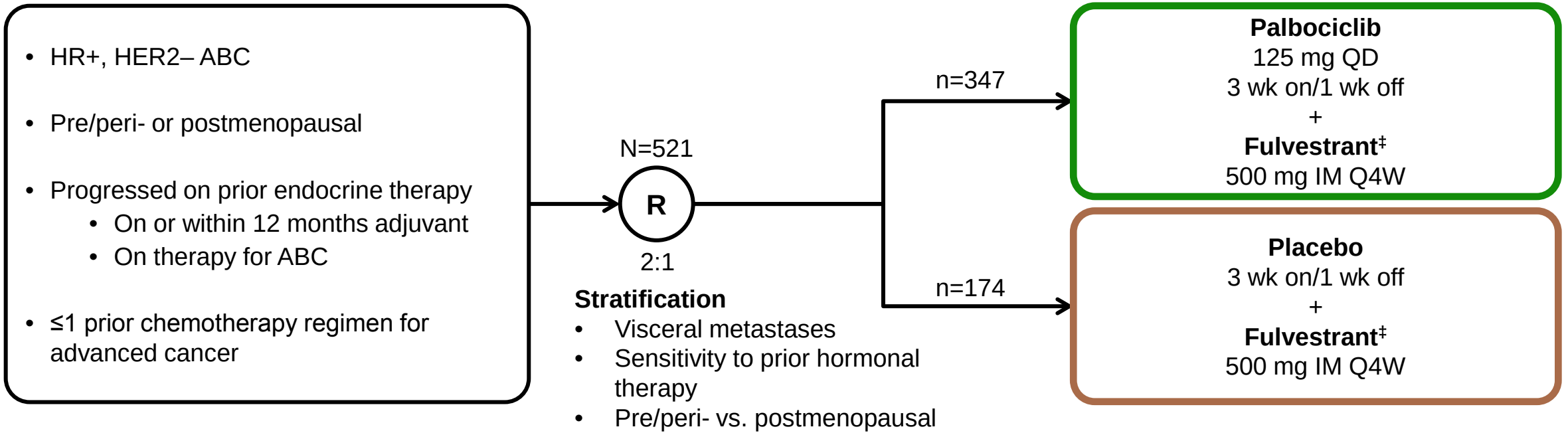
MONALEESA-7 – Conclusion

Erstmals OS Vorteil für einen CDK4/6-Inhibitor zur initialen endokrin-basierten Therapie in der Prämenopause gezeigt

- RIB + ET führte zu einem statistisch signifikant längeren OS vs. ET alleine bei prämenopausalen Frauen mit HR+/HER2– ABC

Mod. Hurvitz SA et al. ASCO 2019, Oral Abstract Session – Breast Cancer – Metastatic, Abstract No. LBA1008

PALOMA-3* – Study Design[1]



- Sensitivity to prior hormonal therapy was defined as documented clinical benefit (CR, PR, or SD ≥24 weeks) to ≥1 prior hormonal therapy regimen in the metastatic setting or ≥24 months of adjuvant hormonal therapy before recurrence.

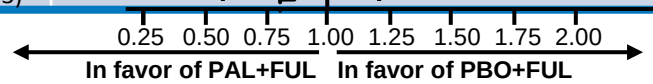
AI, aromatase inhibitor; CR, complete response; IM, intramuscular; PR, partial response; Q4W, once every 4 wk; QD, once daily; SD, stable disease.
*Clinicaltrials.gov, NCT01942135; ‡Administered on days 1 and 15 of cycle 1, then on day 1 of every cycle thereafter. [1]Turner et al. New Engl J Med. 2015.

Mod. Cristofanilli M et al. ESMO 2018, Proffered Paper Session – Presidential Symposium 1, Abstract No. LBA2_PR

PALOMA-3 – Efficacy results

Overall survival by subgroups

Subgroup	Patients, n (%)	HR (95% CI)	PAL+FUL Median OS (95% CI)	PBO+FUL Median OS (95% CI)	Interaction p value
All randomized patients, ITT, stratified	521 (100)	0.81 (0.64-1.03)	34.9 (28.8-40.0)	28.0 (23.6-34.6)	
All randomized patients, ITT, unstratified	521 (100)	0.79 (0.63-1.00)	34.9 (28.8-40.0)	28.0 (23.6-34.6)	
Sensitivity to previous hormonal therapy*					0.12
Yes	410 (78.7)	0.72 (0.55-0.94)	39.7 (34.8-45.7)	29.7 (23.8-37.9)	
No	111 (21.3)	1.14 (0.71-1.84)	20.2 (17.2-26.4)	26.2 (17.5-31.8)	
Site of metastatic disease*					0.44
Visceral	311 (59.7)	0.85 (0.64-1.13)	27.6 (24.4-31.2)	24.7 (20.8-31.8)	
Nonvisceral	210 (40.3)	0.69 (0.46-1.04)	46.9 (39.3-NE)	35.4 (24.6-NE)	
Menopausal status at study entry*					0.25
Pre/peri	108 (20.7)	1.07 (0.61-1.86)	38.0 (24.4-NE)	38.0 (22.2-NE)	
Post	413 (79.3)	0.73 (0.57-0.95)	34.8 (28.8-40.1)	27.1 (22.8-32.1)	
Prior chemotherapy					0.66
Metastatic treatment	177 (34.0)	0.91 (0.63-1.32)	25.6 (21.4-30.1)	26.2 (20.0-37.5)	
None	130 (25.0)	0.68 (0.41-1.15)	46.2 (36.5-NE)	29.7 (22.8-NE)	
Prior lines of therapy in metastatic setting					0.88
0	114 (21.9)	0.70 (0.43-1.14)	36.1 (27.6-43.7)	24.7 (19.5-34.6)	
1	225 (43.2)	0.86 (0.60-1.22)	38.0 (27.2-46.5)	33.8 (23.5-41.4)	
2	131 (25.1)	0.76 (0.48-1.22)	30.0 (23.0-40.1)	24.3 (20.0-29.7)	
≥3	51 (9.8)	0.64 (0.29-1.40)	34.8 (26.1-NE)	27.1 (5.3-NE)	
ESR1 mutation status†					0.60
Positive	106 (20.3)	0.69 (0.43-1.12)	35.6 (23.6-42.0)	24.6 (19.7-33.0)	
Negative	289 (55.5)	0.85 (0.61-1.19)	36.5 (28.0-43.1)	31.8 (22.8-39.1)	
PIK3CA mutation status†					0.64
Positive	133 (25.5)	0.74 (0.48-1.14)	28.6 (25.3-39.3)	22.2 (15.7-29.5)	
Negative	262 (50.3)	0.84 (0.59-1.18)	38.8 (28.9-44.5)	33.0 (24.3-41.6)	



ESR1, estrogen receptor 1; NE, not estimable; PIK3CA, phosphatidylinositol 3-kinase, catalytic subunit alpha.
*Prespecified stratification factors. †ESR1 and PIK3CA data were from a subset of patients who had circulating tumor DNA samples and who were tested for the mutations.

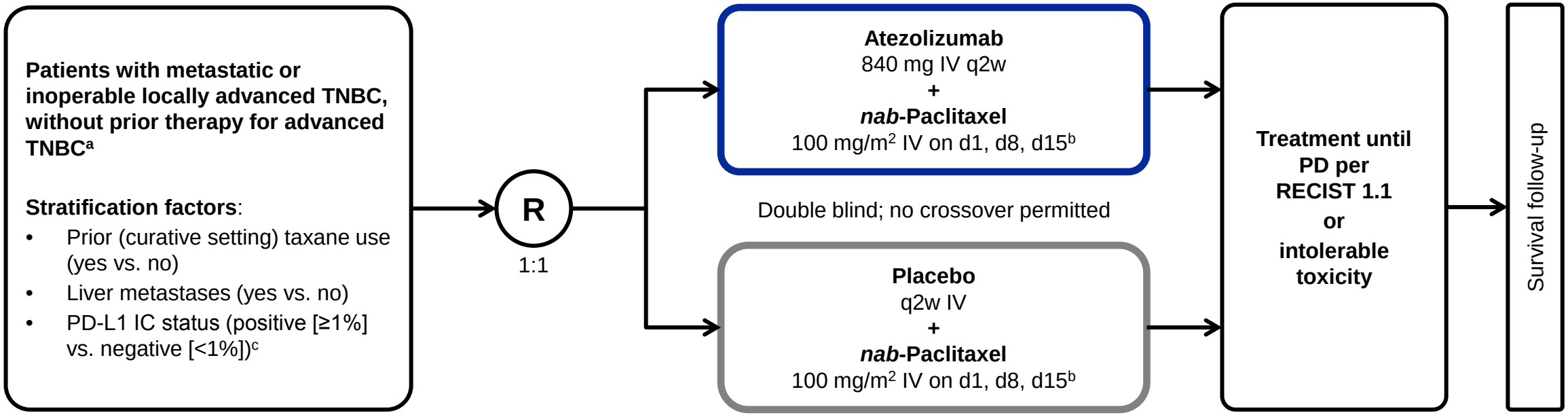
Mod. Cristofanilli M et al. ESMO 2018, Proffered Paper Session – Presidential Symposium 1, Abstract No. LBA2_PR

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*

Schmid P et al. Oral Abstract Session – Breast Cancer – Metastatic
(discussed by: Santa-Maria CA)

Abstract No. 1003

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+

[a]Prior chemotherapy in the curative setting allowed if treatment-free interval ≥12 months. [b]28-day cycle. [c]Centrally evaluated per VENTANA SP142 IHC assay. [d]Efficacy endpoints assessed by investigators per RECIST 1.1. NCT02425891. RECIST, Response Evaluation Criteria in Solid Tumors.

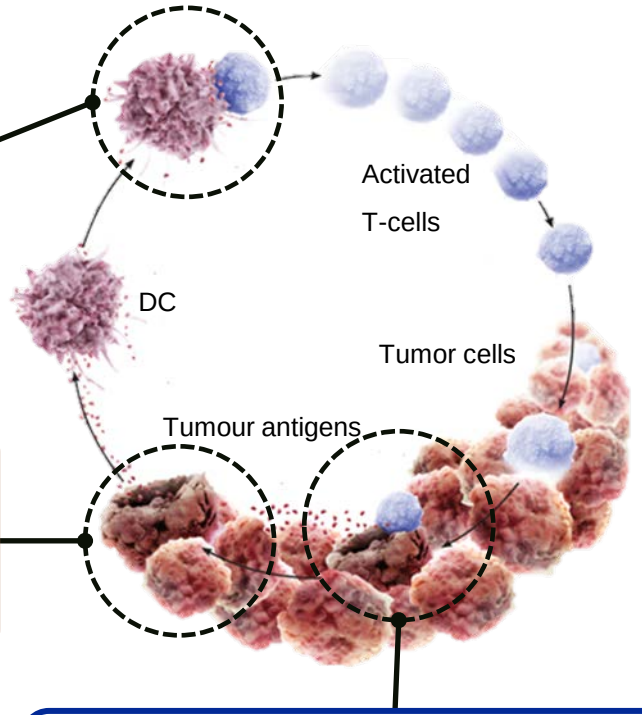
Mod. Schmid P et al. ASCO 2019, Oral Abstract Session – Breast Cancer – Metastatic, Abstract No. 1003

IMpassion130 – Background

Atezolizumab and Chemotherapy

Atezolizumab:
Promotes T-cell activation[1]

Chemotherapy:
Promotes DC recruitment to the site of cell death[2,3]



Atezolizumab:
Restores anti-cancer immunity,[1] with activity further enhanced by chemotherapy-induced antigen exposure

- Atezolizumab (anti-PD-L1) monotherapy is approved in the United States, Europe and elsewhere for certain types of metastatic urothelial carcinoma and lung cancer[4]
- In a Phase I study, Atezolizumab monotherapy was active in multiple cancers, including TNBC,[5,6] with greater activity in patients whose tumours had PD-L1 IC ≥ 1%[6]
- The addition of chemotherapy can enhance Atezolizumab's anti-tumour activity[7,8]
  - In a Phase Ib study in mTNBC, concurrent administration of nab-Paclitaxel did not inhibit Atezolizumab-mediated immunodynamic effects[8]

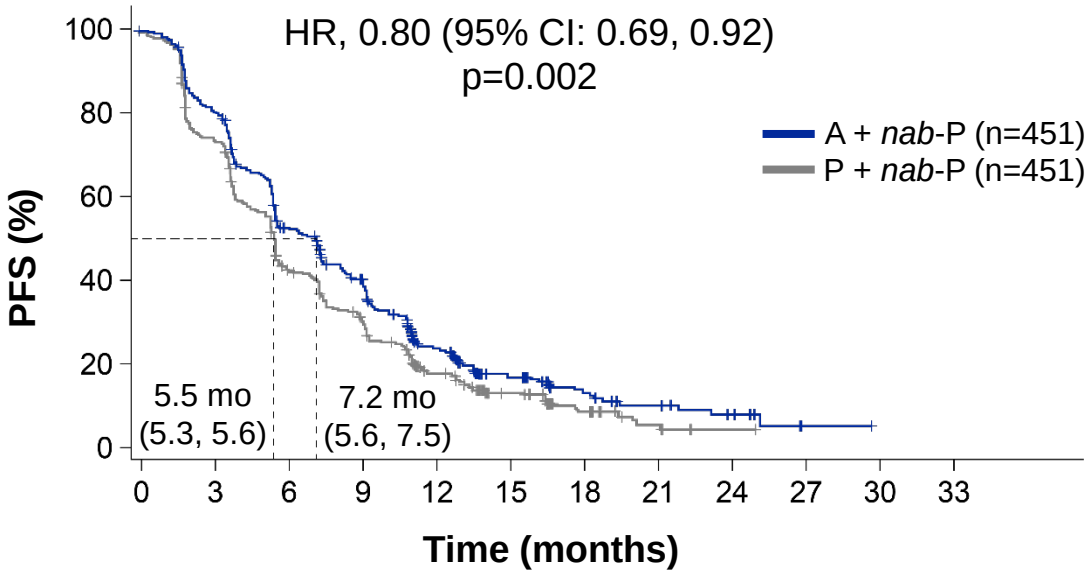
DC, dendritic cell.
1Chen Immunity 2013. 2Zitvogel Immunity 2013. 3Emens CIR 2015.
4TECENTRIQ US PI/SmPC 2018. 5Herbst Nature 2014. 6Emens JAMA Oncol 2018. 7Jotte ASCO 2018. 8Pohlmann AACR 2018.

Mod. Schmid P et al. ESMO 2018, Proffered Paper Session – Presidential Symposium 1, Abstract No. LBA1_PR

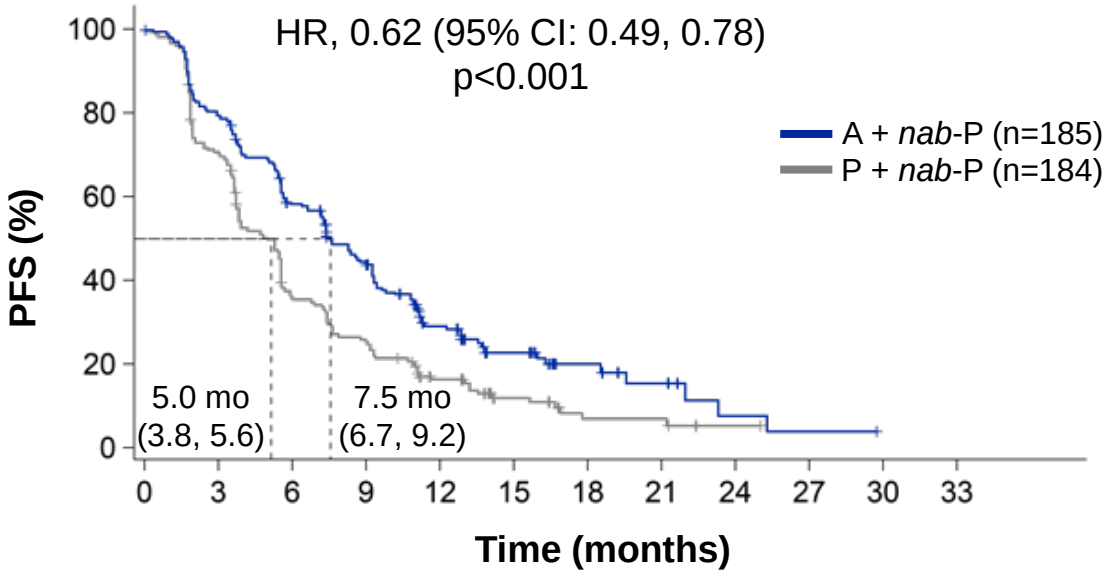
IMpassion130 – Primary PFS Analysis

ITT and PD-L1 IC+ Subgroup

ITT Population



PD-L1 IC+ Subgroup

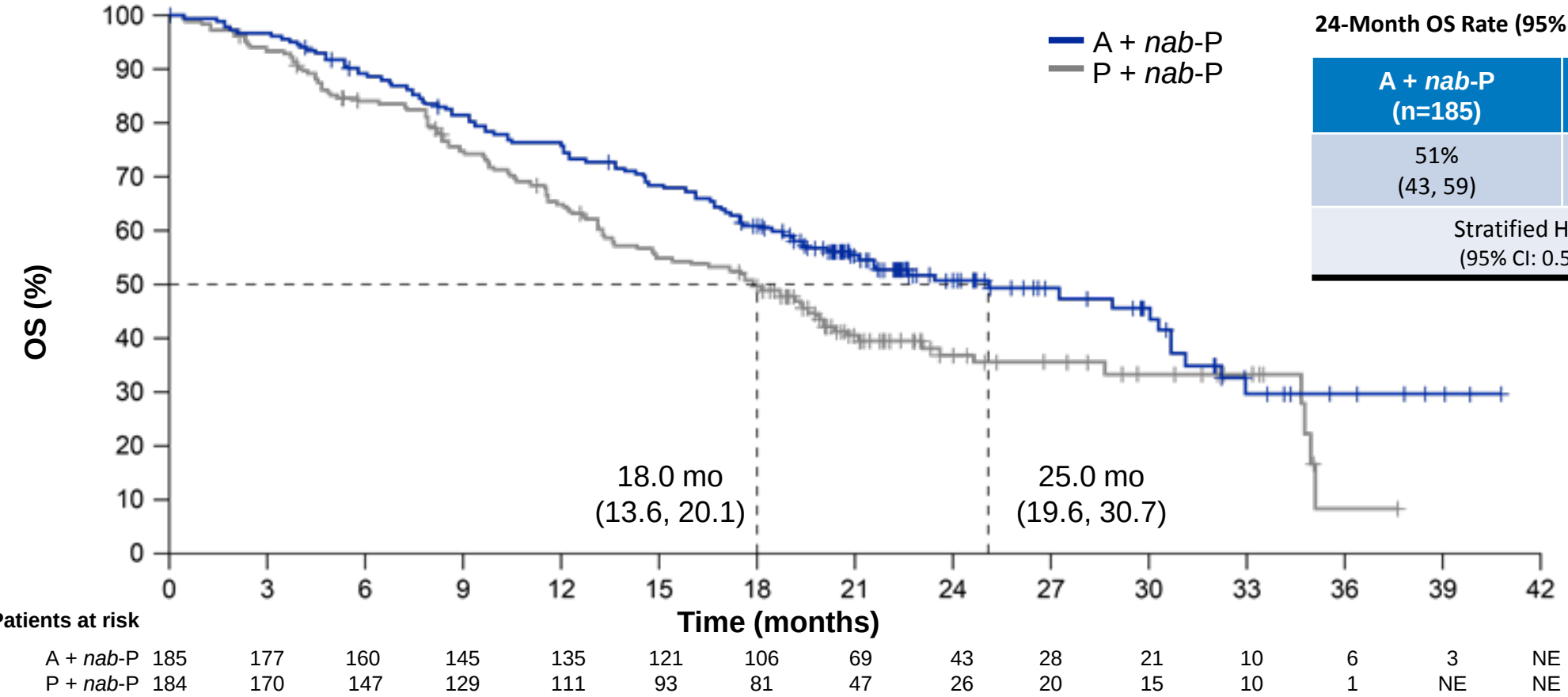


- PFS benefit driven by PD-L1 IC+ patients, as a treatment effect was not observed in PD-L1 IC– patients[1]
- Based on these data,[2] Atezolizumab + *nab*-Paclitaxel received accelerated approval by the FDA[3] and is recommended for patients with PD-L1 IC+ mTNBC in the NCCN[4] and AGO[5] guidelines

A, Atezolizumab; HR, hazard ratio; *nab*-P, *nab*-Paclitaxel; P, Placebo. Data cutoff: April 17, 2018. Median follow-up (ITT): 12.9 months.
1. Emens SABCS 2018. 2. Schmid *New Engl J Med.* 2018. 3. Tecentriq (Atezolizumab) [package insert]. South San Francisco, CA: Genentech USA, Inc; 2019
4. NCCN Clinical Practice Guidelines. Breast Cancer. V1.2019. 5. AGO Guidelines Breast Version 2019.1.

Mod. Schmid P et al. ASCO 2019, Oral Abstract Session – Breast Cancer – Metastatic, Abstract No. 1003

IMpassion130 – OS in PD-L1+ Population



24-Month OS Rate (95% CI)

A + *nab*-P (n=185)	P + *nab*-P (n=184)
51% (43, 59)	37% (29, 45)
Stratified HR, 0.71[a] (95% CI: 0.54, 0.93)	

Patients at risk

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

[a]Not formally tested due to pre-specified hierarchical analysis plan.
Clinical cutoff date: January 2, 2019. Median PFS (95% CI) is indicated on the plot. Median FU (ITT): 18.0 months..

Mod. Schmid P et al. ASCO 2019, Oral Abstract Session – Breast Cancer – Metastatic, Abstract No. 1003

IMpassion130 – Conclusion

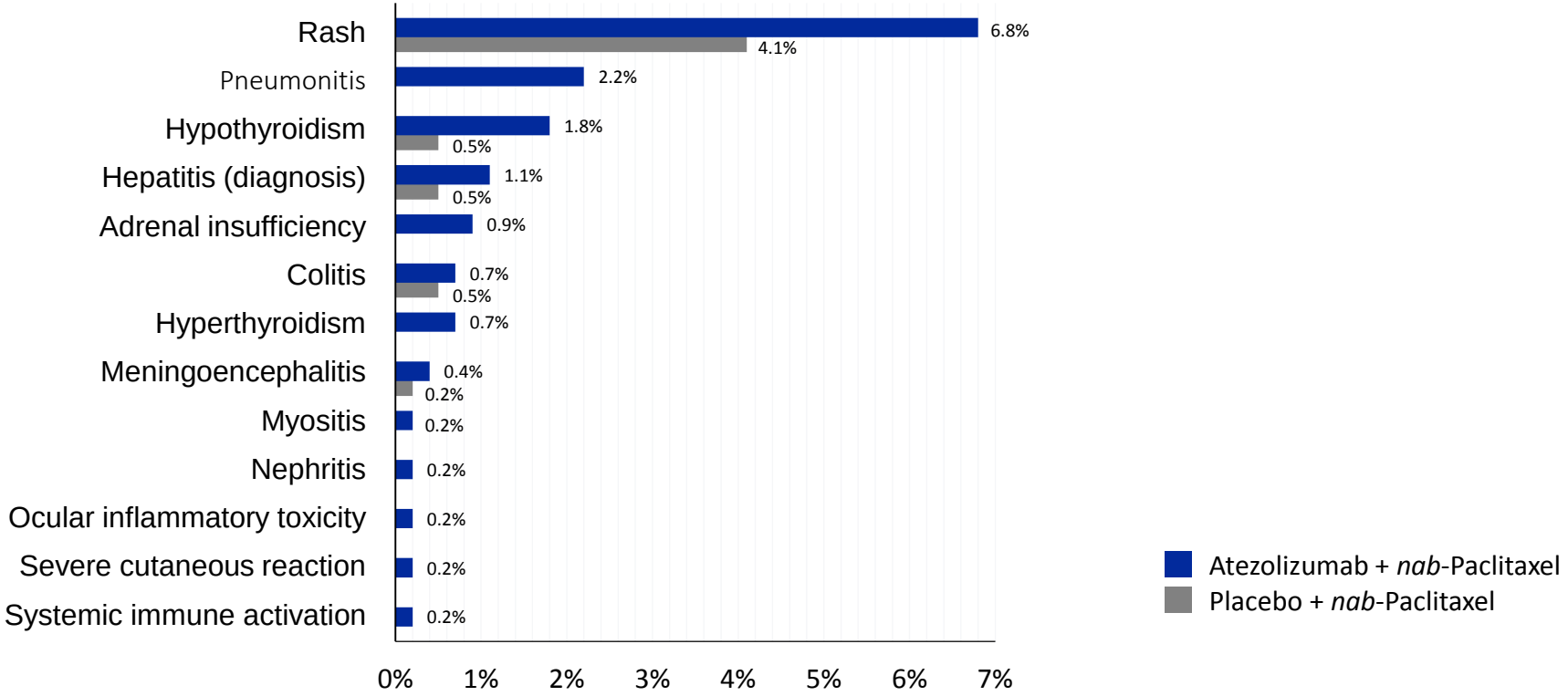
- Klinisch relevanter OS Vorteil unter Atezo + *nab*-Paclitaxel in der 2. IMpassion130-Analyse bei nicht-vorbehandelten PD-L1+ mTNBC-Patienten

Mod. Santa-Maria CA. ASCO 2019, Oral Abstract Session – Breast Cancer – Metastatic, Discussing Abstracts 1003, 1004, 1005

IMpassion130 – Results

Immune-Mediated AESI[a] Requiring Systemic Corticosteroids

Rash and pneumonitis were the only AESI requiring systemic corticosteroid use in ≥10 patients in the Atezolizumab + *nab*-Paclitaxel arm.



[a]Grouped MeDRA preferred terms.

Mod. Schneeweiss A et al. ASCO 2019, Poster Session – Breast Cancer – Metastatic, Abstract No. 1068