SABCS 2015: Triple Negative Breast Cancer

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San Antonio Breast Cancer Symposium – December 8-12, 2015

Early survival analysis of the randomized phase II trial investigating the addition of carboplatin to neoadjuvant therapy for triple-negative and HER2-positive early breast cancer (GeparSixto)

Gunter von Minckwitz, Sibylle Loibl, Andreas Schneeweiss, Christophe Salat, Eric Hahnen, Mahdi Rezai, Dirk Michael Zahm, Peter Klare, Jens Uwe Blohmer, Hans Tesch, Fariba Khandan, Peter Fasching, Christian Jackisch, Rita Schmutzler, Valentina Nekljudova, Michael Untch

for the

GBG/AGO-B study groups

AGO-B BREAST STUDY GROUP

GBG GERMAN BREAST GROUP

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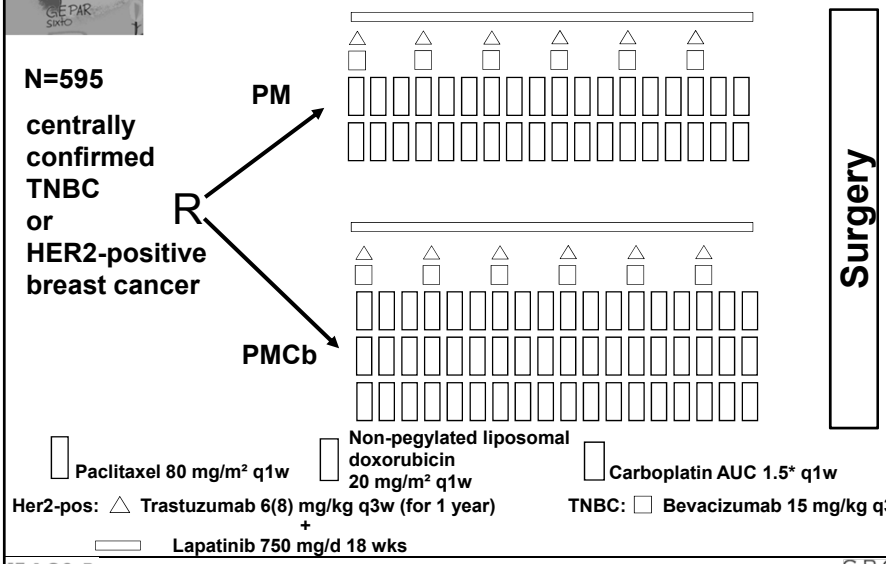
Subtype Specific Targeted Therapy



*reduced from AUC 2 at amendment 1 after enrolment of 330 patients

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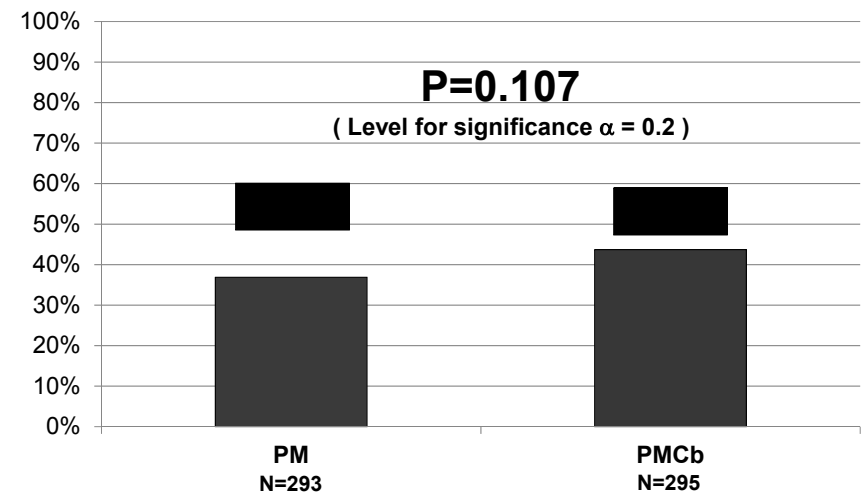
Primary Endpoint: pCR



von Minckwitz et al. Lancet Oncology 2014

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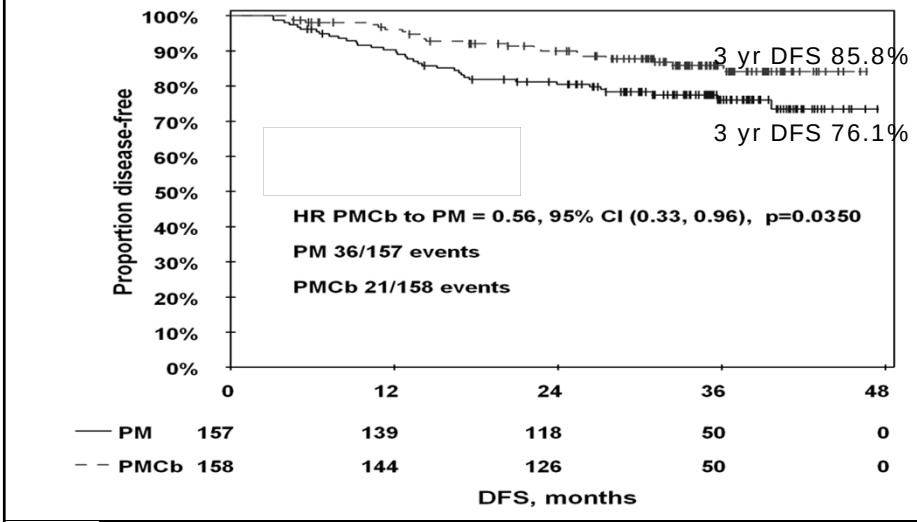
Effect of Carboplatin in Patients with TNBC



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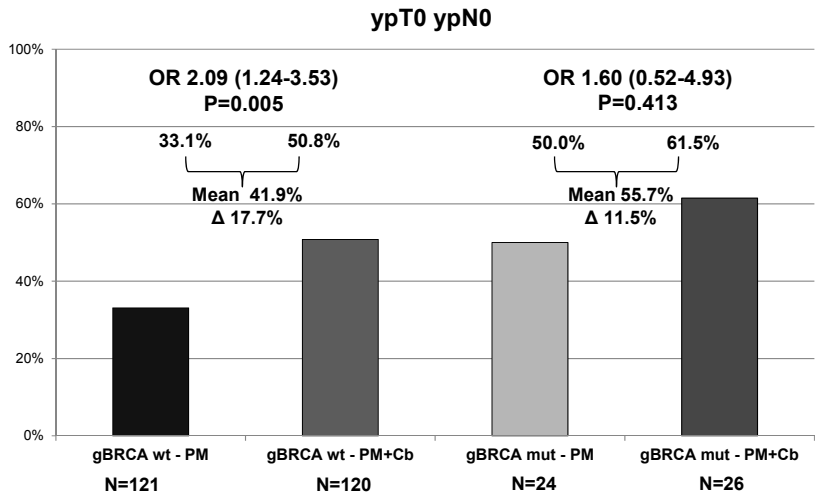
pCR Rates by g*BRCA* Status and Carboplatin Treatment in Patients with TNBC



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von Minckwitz G et al., ASCO 2014, updated data; E. Hahnen in prep.

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Conclusion

- **Carboplatin induces a significantly (HR=0.56, p=0.035) improved disease-free survival in patients with TNBC but not in patients with HER2-positive disease (HR 1.33, p=0.372) (Interaction Test p=0.046).**
- **Survival effect of carboplatin was correctly predicted by its effect on pCR, supporting surrogacy of pCR in case of large pCR differences (like NOAH trial).**
- **Addition of carboplatin appeared more relevant (pCR and DFS) for patients with *wt gBRCA.* We hypothesize that the DNA damaging effect of non-pegylated doxorubicin is already sufficient in highly DNA instable mutant *gBRCA* tumors, so that no additional effect of carboplatin can be demonstrated in this subgroup. The potential impact of bevacizumab in GeparQuinto will be elucidated by P. Fasching on Friday at 10.45 am.**
- **Prognostic information of pCR was confirmed also in patients with mt *gBRCA*.**
- **Overall, survival analysis of the GeparSixto study support the use of carboplatin as part of neoadjuvant treatments in patients with TNBC.**

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Event-free and overall survival following neoadjuvant weekly paclitaxel and dose-dense AC +/- carboplatin and/or bevacizumab in triple-negative breast cancer: outcomes from CALGB 40603 (Alliance)

William M Sikov, Donald A Berry, Charles M Perou, Baljit Singh, Constance T Cirrincione, Sara M Tolaney, George Somlo, Elisa R Port, Rubina Qamar, Keren Sturtz, Eleftherios Mamounas, Mehra Golshan, Jennifer R Bellon, Deborah Collyar, Olwen M Hahn, Lisa A Carey, Clifford A Hudis, Eric P Winer for the CALGB/Alliance

ALLIANCE FOR CLINICAL TRIALS IN ONCOLOGY

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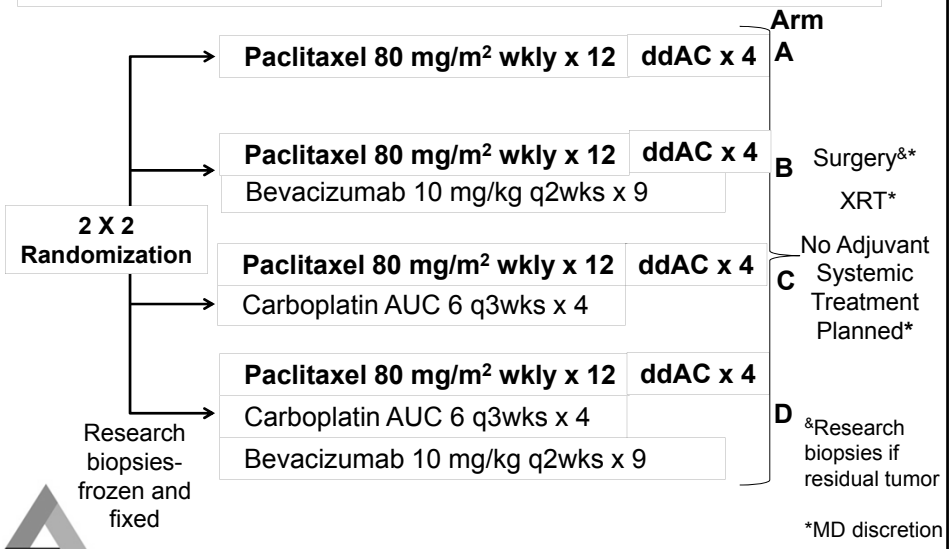
CALGB 40603: Schema – Randomized Phase II



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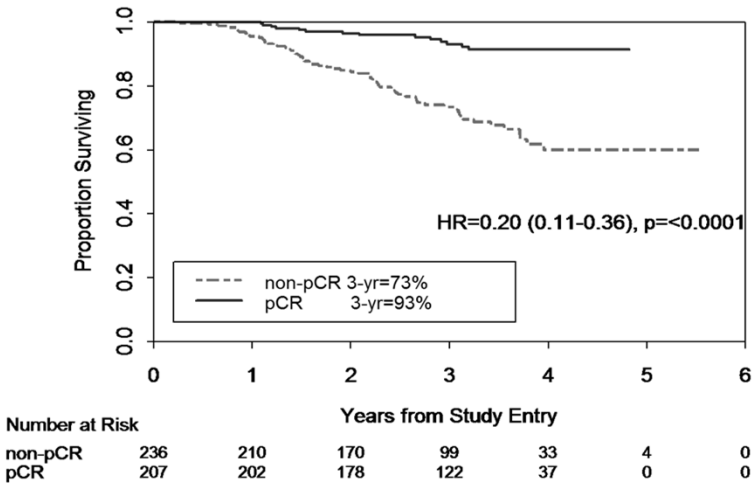
CALGB 40603 – OS by pCR Breast/Axilla



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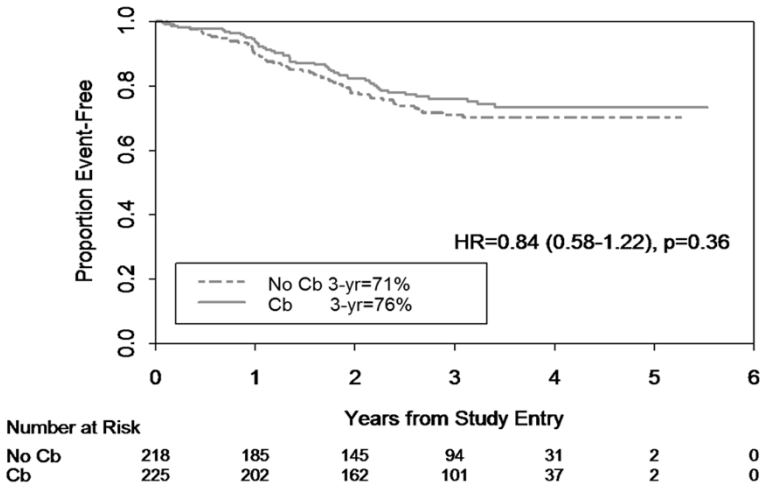
CALGB 40603 – EFS for carboplatin vs. not



Number at Risk

No Cb	218	185	145	94	31	2	0
Cb	225	202	162	101	37	2	0

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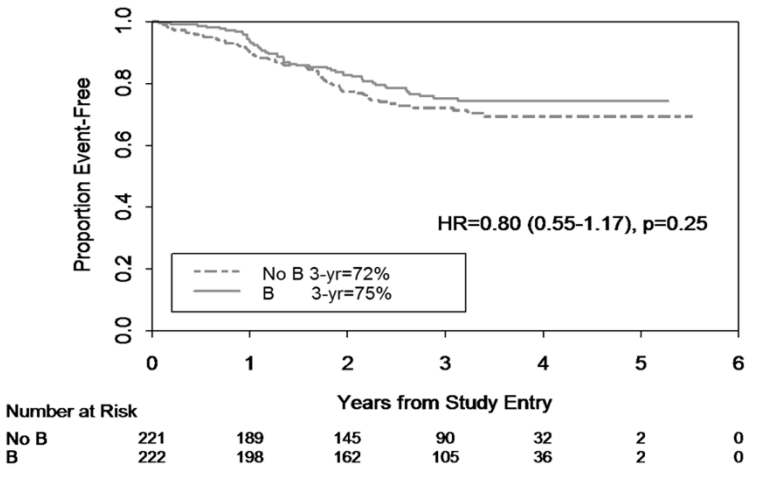
CALGB 40603 – EFS for bevacizumab vs. not



Number at Risk

No B	221	189	145	90	32	2	0
B	222	198	162	105	36	2	0

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CALGB/Alliance 40603: Conclusions

- Achievement of a pCR with weekly paclitaxel followed by ddAC +/- carboplatin and/or bevacizumab is associated with significant improvements in EFS and OS
  - Substantial reductions are seen in both LRR and DR
  - Inferior outcomes are seen in clinical stage III disease with failure to achieve a pCR and in clinically node-positive patients with persistently positive axillary LNs after NACT

  Results are consistent with the FDA-requested meta-analysis
- EFS and OS Hazard Ratios were lower for pCR Breast/Axilla than for pCR Breast, but the addition of RCB I patients did not diminish the prognostic significance of achieving pCR Breast/Axilla

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CALGB/Alliance 40603: Conclusions

- Our study was underpowered to determine whether the increases in the pCR rates seen with the addition of carboplatin and bevacizumab improve EFS or OS
- Previous studies (BEATRICE, E5103, GeparQuinto, NSABP B-40) have failed to demonstrate improvements in long-term outcomes (EFS, RFS or OS) in stage I-III TNBC with the addition of bevacizumab to a control (neo)adjuvant chemotherapy regimen

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CALGB/Alliance 40603: Conclusions

- Results from other completed (GeparSixto) and ongoing (BrighTNess, NRG-003) studies in the neoadjuvant and adjuvant settings should help to clarify whether the addition of carboplatin benefits patients with early stage TNBC
- Despite the significantly higher pCR rates seen in CALGB 40603, neither carboplatin nor bevacizumab have been shown to improve RFS or OS when administered as part of neoadjuvant therapy in stage II-III TNBC

Comparison of 12 weeks neoadjuvant Nab-Paclitaxel combined with Carboplatinum vs. Gemcitabine in triple-negative breast cancer: WSG-ADAPT TN randomized phase II trial

Gluz O, Nitz U, Liedtke C, Christgen M, Grischke E, Forstbauer H, Braun M, Warm M, Hackmann J, Uleer C, Aktas B, Schumacher C, Bangemann N, Lindner C, Kümmel S, Clemens M, Potenberg J, Staib P, Kohls A, Sotlar K, Pelz E, Kates RE, Würstlein R, Kreipe H, Harbeck N. on behalf of the ADAPT investigators

West German Study Group, Moenchengladbach; Bethesda Hospital, Moenchengladbach; University Hospital Schleswig-Holstein, Camus Lübeck; Institut of Pathology, MHH, Hanover; University Hospital Tübingen, Oncological practice Troisdorf, Clinics Rotkreuz, Munich, Clinics Holweide, Cologne, Marienhospital Witten; Gynecological Practice, Hildesheim, University Hospital, Essen; St. Elisabeth Clinics, Cologne, University Hospital Charite, Berlin, Diakonie Clinics, Hamburg, Cinics Essen-Mitte, Hospital Mutterhaus, Trier; Evangelical Waldkranknehaus, Berlin, St. Antonius Hospital, Eschweiler, Insitite of Pathology, Viersen Ludwig Maximilian University Clincs Munich

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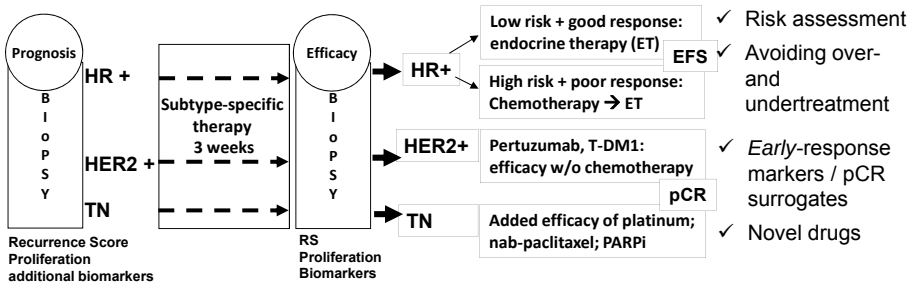
Adjuvant Dynamic marker-Adjusted Personalized Therapy trial (ADAPT)

WSG WOMEN'S HEALTHCARE STUDY GROUP

ADAPT

umbrella trial, n ~ 5,000



- ✓ Risk assessment
- ✓ Avoiding over- and undertreatment
- ✓ *Early*-response markers / pCR surrogates
- ✓ Novel drugs

WSG AM06 Principal Investigators: Nadia Harbeck (LKP), Munich; Ulrike Nitz, Mönchengladbach, Germany.

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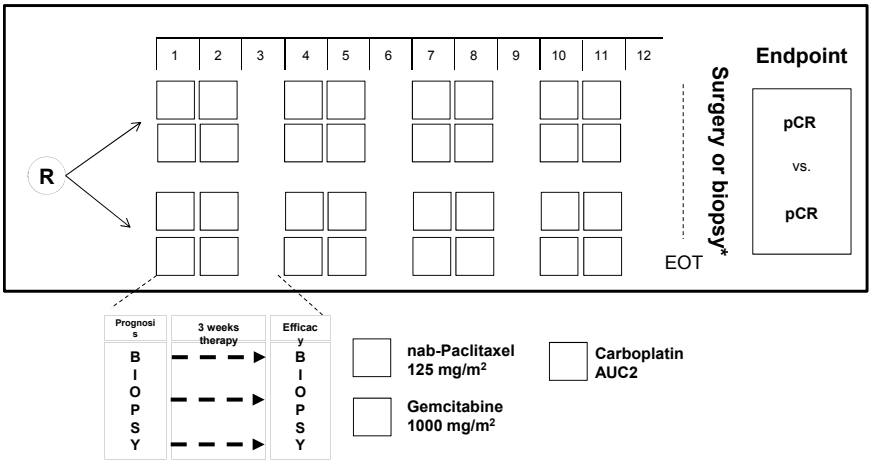
ADAPT HR-/HER2-: Trial Design

WSG WOMEN'S HEALTHCARE STUDY GROUP

ADAPT



Standard chemotherapy (4xEC) recommended after surgery / 12-week biopsy (in case of clinical non-pCR)

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ADAPT HR-/HER2-: Baseline characteristics

		Nab-Pac/Gem	Nab-Pac/Carbo
n		182	154
Age	median (range)	50 (26-75)	52 (29-76)
cT	1	68 (37.4%)	57 (37%)
	≥2	114 (62.6%)	97 (62.9%)
cN	0	135 (74.2)	113 (73.4%)
	≥1	47 (25.8%)	41 (26.6%)
Ki-67	median	75%	70%
Central grade 3		172 (94.5%)	140 (90.9%)

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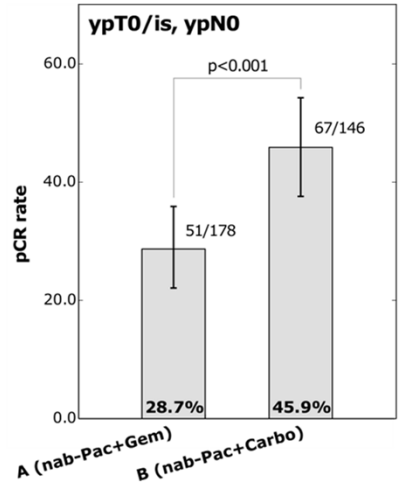
ADAPT HR-/HER2-: Pathological complete response



ADAPT HR-/HER2-: Conclusions

- **Nab-Pac/Carbo is associated with less toxicity and significant superiority to Nab-Pac/Gem in terms of pCR**
- **Early morphological changes seem to be predictive for pCR, irrespective of treatment arm**
- **No predictive factors for carboplatin efficacy have been identified so far; further correlative analyses (e.g. subtypes, family history, BRCA1-ness etc.) are ongoing**
- **Validation of these results in larger studies seems warranted**

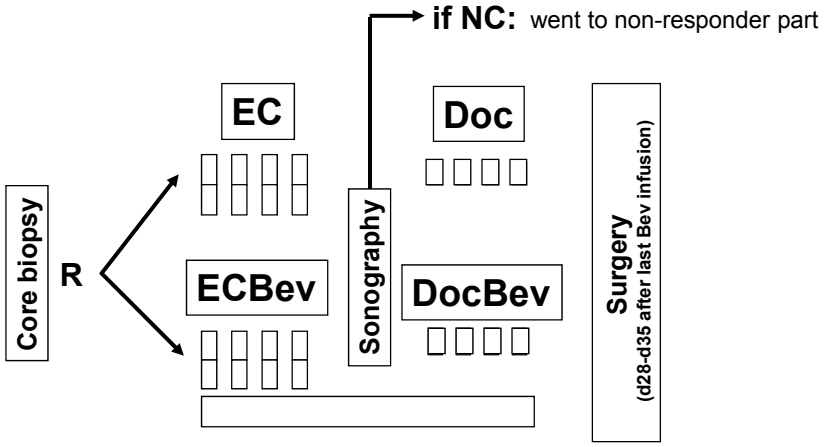
BRCA mutations, therapy response and prognosis in the neoadjuvant GeparQuinto Study .

Peter A. Fasching, Sibylle Loibl, Holger Eidtmann, Hans Tesch, Michael Untch, Jörn Hilfrich, Christian Schem, Mahdi Rezai, Bernd Gerber, Serban Dan Costa, Jens-Uwe Blohmer, Tanja Fehm, Jens Huober, Cornelia Liedtke, Volkmar Müller, Valentina Nekljudova, Karsten E Weber, Brigitte Rack, Matthias Rübner, Liewei Wang, James N Ingle, Richard M Weinshilboum, Gunter von Minckwitz and Fergus Couch

for the

GBG/AGO-B study groups

HER2-negative part



E: Epirubicin 90 mg/m² **Doc:Docetaxel 100mg/m²**
C: Cyclophosphamide 600 mg/m² **Bev: Bevacizumab 15 mg/kg**
(all 3 week cycles)

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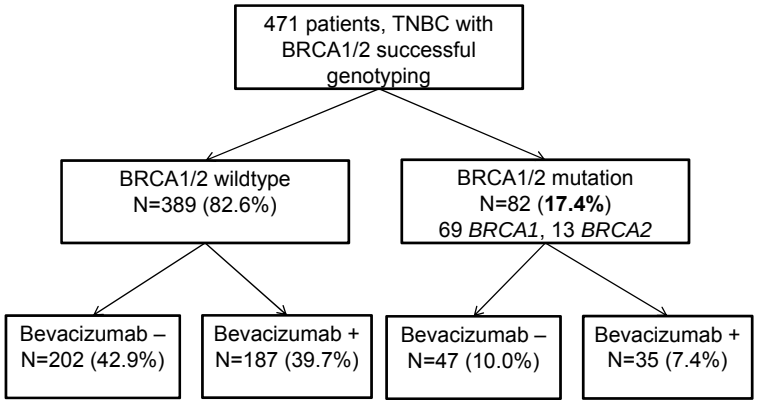
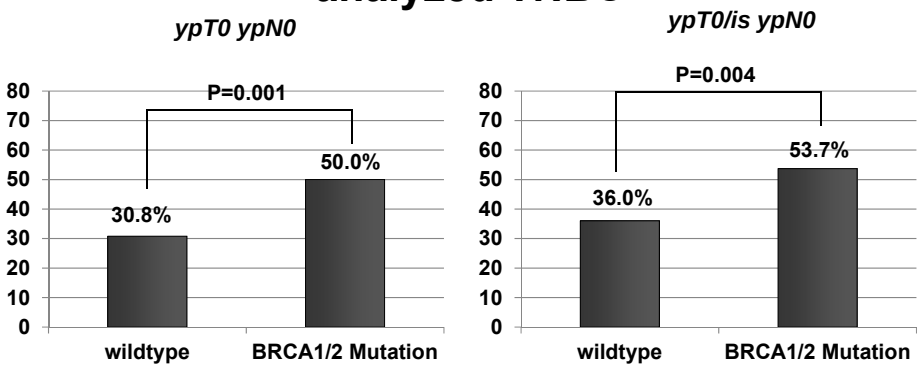
BRCA1/2 Mutations and distribution over treatment arms



Results: *BRCA1/2* mutations and pCR in all analyzed TNBC



- **Results seem to be consistently similar for *BRCA1* and *BRCA2* mutation carriers, when analyzed seperatly, however very small sample sizes**

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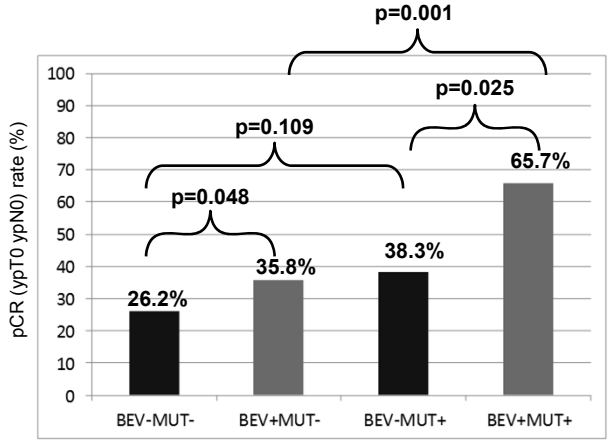
Results exploratory analysis pCR according to randomization arms



p (interaction) = 0.1912

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Conclusion

- **Patients with *BRCA1* or *BRCA2* mutations have significantly higher pCR rates after a neoadjuvant chemotherapy.**
- **The effect seems to be stronger in patients treated with bevacizumab.**
- ***BRCA1/2* mutations had a marginal effect on prognosis.**
- **The effect of pCR on prognosis was smaller in patients with a *BRCA1/2* mutation, than in patients with wildtype genotype, but test for interaction was not significant.**
- **Taken the results from GeparSixto into consideration (von Minckwitz et al., Presentation S3-04), effects of *BRCA1/2* mutation status on pCR and prognosis might be highly dependent on given therapies.**

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SUCCESS

Persistence of circulating tumor cells in high risk early breast cancer patients during follow-up care suggests poor prognosis: Results from the adjuvant SUCCESS A trial

Wolfgang Janni, Brigitte Rack, Peter A Fasching, Lothar Haeberle, Thomas WP Friedl, Hans Tesch, Ralf Lorenz, Julia Neugebauer, Julian Koch, Bernadette Jaeger, Tanja Fehm, Volkmar Mueller, Andreas Schneeweiß, Werner Lichtenegger, Matthias W Beckmann, Christoph Scholz, Klaus Pantel, Elisabeth Trapp

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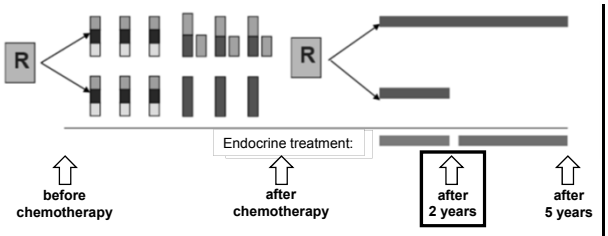
SUCCESS

SUCCESS A – study design



Blood sampling for CTC assessment

First randomization:
3 cycles FEC100 followed by 3 cycles docetaxel vs. 3 cycles FEC100 followed by 3 cycles docetaxel plus gemcitabine

Second randomization:
2 years vs. 5 years of zoledronate

5- FU 500 mg/m², Epirubicin 100 mg/m², Cyclophosphamide 500 mg/m² q3w

Docetaxel 100 mg/m² q3w

Docetaxel 75 mg/m², Gemcitabine 1.000 mg/m² d1,8 q3w

Zoledronate 4mg x 2a vs 5a (q3mx24m, vs q3mx24m followed by q6mx36m)

Tamoxifen 20 mg qid p.o. x 2a (plus Goserelin 3.6 mg depot x 2a in premenopausal pts

Anastrozole 1 mg qid p.o. x 3a in postmenopausal pts (Tam in premenopausal pts)

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SUCCESS

Patient characteristics

FT2

- **3754** patients with high-risk early breast cancer (defined as pN1-3, or pT2-4, or G3, or hormone receptor negative, or age ≤ 35) randomized for SUCCESS A
- Data from **1087 patients** with CTC determination both before and two years after chemotherapy **available for analysis**
- No significant differences with regard to patient and tumor characteristics between the 1087 patients included and the remaining 2667 patients (all $p > 0.05$)

Slide 30

FT2 von mir hinzugefügt...
Friedl Thomas, 12/1/2015

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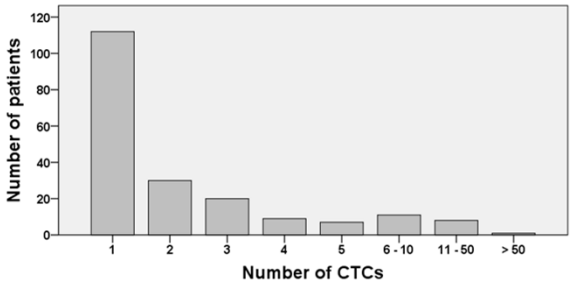
SUCCESS

Results I: Prevalence of CTCs after two years

198 (18.2%) of the 1087 patients with at least one CTC in the blood two years after adjuvant chemotherapy (median 1 CTC, range 1 – 99 CTCs)



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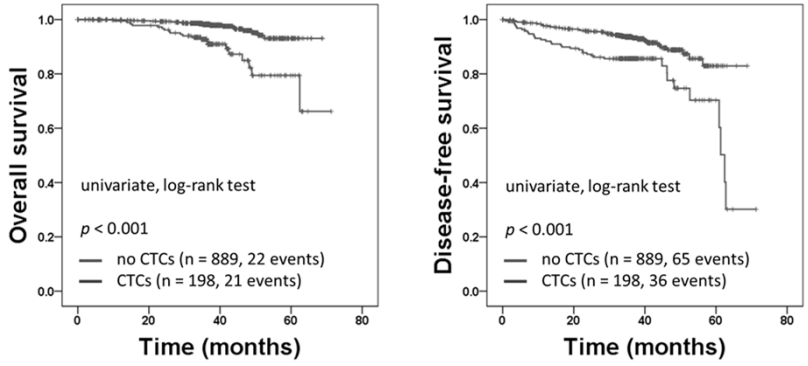
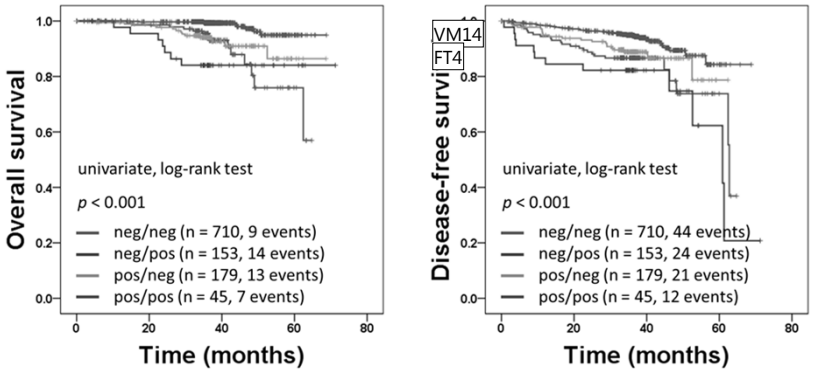
Results IV: Prognostic value of CTCs assessed two years after adjuvant chemotherapy



SUCCESS

Results V: Subgroups – CTC status before and two years after adjuvant chemotherapy



SUCCESS

Summary

- 198 (18.2%) of 1087 patients with at least one CTC in the blood two years after adjuvant chemotherapy
- **Presence of CTCs two years after adjuvant chemotherapy is a significant independent prognostic factor for poor OS and DFS**
- Patients with CTCs both before and two years after adjuvant chemotherapy had worst survival outcome
- The prognostic value of the presence of CTCs two years after chemotherapy was not evident for patients with HER2-positive tumors (but no significant interaction between presence of CTCs two years after adjuvant chemotherapy and biological subtype)

Slide 33

VM14 Da die Beshriftung eher an die Kurven, ist so nicht schnell genug zu erfassen denke ich
Volkmar Müller, 11/30/2015

FT4 sehe ich problematisch - ich wüsste nicht, wie man die Beschriftungen zu den Kurven platziert ohne dass es sehr unübersichtlich wird...
Friedl Thomas, 12/1/2015

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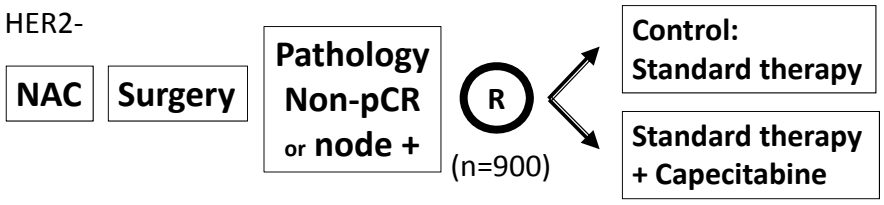
A phase III trial of adjuvant capecitabine in breast cancer patients with HER2-negative pathologic residual invasive disease after neoadjuvant chemotherapy (CREATE-X/JBCRG-04)

Capecitabine for REsidual cancer as Adjuvant ThErapy

Lee S-J[1], Toi M[2], Lee E-S[3], Ohtani S[4], Im Y-H[5], Im S-A[6], Park B-W[7], Kim S-B[8], Yanagita Y[9], Takao S[10], Ohno S[11], Aogi K[12], Iwata H[13], Kim A[14], Sasano H[15], Yokota I[16], Ohashi Y[17] and Masuda N[18]

[1]Yeungnam University Hospital; [2]Kyoto University Hospital; [3]National Cancer Center; [4]Hiroshima City Hospital; [5]Samsung Medical Center; [6]Seoul National University Hospital; [7]Severance Hospital, Yonsei University College of Medicine; [8]Asan Medical Center; [9]Gunma Prefectural Cancer Center; [10]Hyogo Cancer Center; [11]National Kyusyu Cancer Center; [12]NHO Shikoku Cancer Center; [13]Aichi Cancer Center; [14]Korea University Guro Hospital; [15]Tohoku University; [16]Kyoto Prefectural University of Medicine; [17]Chuo University and [18]NHO Osaka National Hospital

CREATE-X: Trial Design

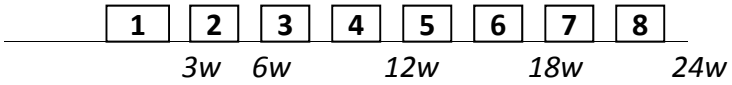


Stratification factors:
ER, Age, NAC, ypN,
5FU and institution

Standard therapy:
HR+: Hormone therapy
HR-: No further systemic treatment

Capecitabine Therapy

Capecitabine (X): 2,500 mg/m^2/day, po, day 1-14
Repeat every 3 weeks for 8 cycles



According to the safety interim analysis of the first 50 pts treated with 6 cycles of X, the IDMC recommended extending X to 8 cycles.

Compliance of capecitabine

Total (N=439)	Cases planned for 6 cycles (N=159)	Cases planned for 8 cycles (N=280)
Completion	92 (58.0)	106 (37.9)
Reduction	38 (23.9)	104 (37.1)
Discontinued	29 (18.2)	70 (25.0)
RDI* (%) Mean (SD)	87.9 (21.6)	79.1 (29.0)

* RDI: Relative dose intensity

Safety

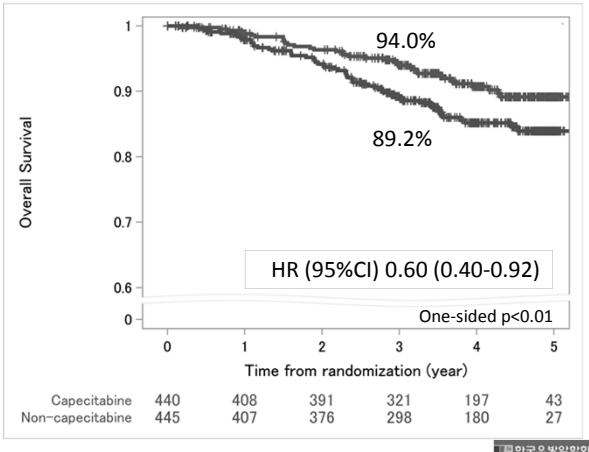
≥G3 (N, %)	Capecitabine arm (N=440)		Control arm (N=445)	
Neutropenia *	29	(6.6)	7	(1.6)
Diarrhea *	13	(3.0)	2	(0.4)

- significantly higher in the capecitabine arm
  (Neutropenia: p<0.001, Diarrhea: p=0.004)
- All grade incidence is significantly higher in the capecitabine arm as below,
  Leucopenia, Neutropenia, Anemia, Thrombocytopenia
  Elevated AST/ALT, Total bilirubin
  Appetite loss, Diarrhea, Stomatitis and Fatigue

Capecitabine administrated Hand-Foot-Syndrome (N=440)		
Grade 0	122	(27.7)
Grade 1	160	(36.4)
Grade 2	110	(25.0)
Grade 3	48	(10.9)
Grade 1-3	318	(72.3)

Ohtani S, et al. SABCS2013#P3-12-03

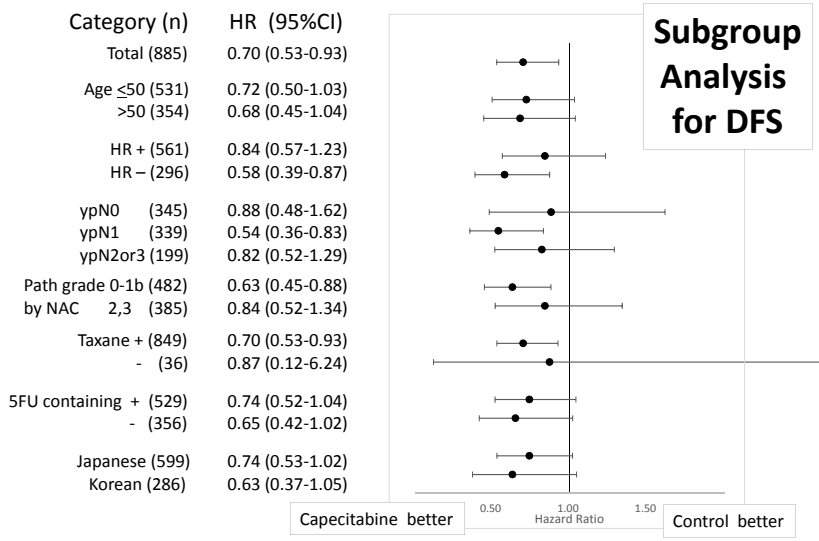
Overall Survival



5yr OS

89.2% Capecitabine

83.9% Control



Conclusions

- After standard neoadjuvant chemotherapy containing A and/or T, postoperative adjuvant use of capecitabine improved DFS significantly in HER2-negative primary breast cancer patients with pathologically proven residual invasive disease.
- OS was significantly improved by capecitabine adjuvant therapy for non-pCR or node-positive patients after NAC.
- The balance of benefit and toxicity would favor the use of capecitabine in the post-NAC situation, but prediction for the therapeutic benefit needs to be investigated further.
- The cost-effectiveness analysis will be carried out.

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Avelumab (MSB0010718C), an anti-PD-L1 antibody, in patients with locally advanced or metastatic breast cancer: a phase Ib JAVELIN Solid Tumor trial

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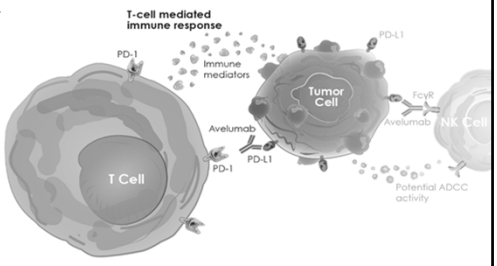
Avelumab* (MSB0010718C)

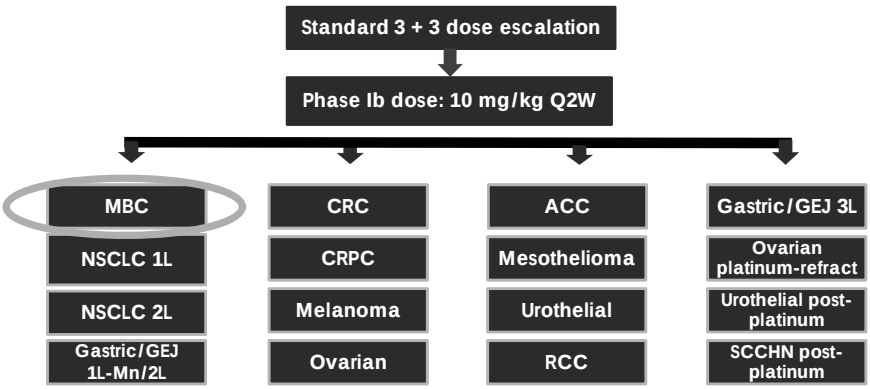
- Fully human anti-PD-L1 IgG1 antibody[1]
- Binds PD-L1[1]
  - Inhibits PD-1/PD-L1 interactions
  - Leaves PD-1/PD-L2 pathway intact
- Half-life ≈4-5 days; >95% TO over whole 2-week dosing period at 10 mg/kg dose[2]
- ADCC may contribute to activity, as shown in preclinical models[3]
- Doses up to 20 mg/kg Q2W safely administered[1,2]
- Antitumor activity in patients with lung, gastric, ovarian, bladder, and other malignancies, all unselected for PD-L1 expression[4-7]



* Avelumab is the proposed international nonproprietary name (INN) for the anti-PD-L1 monoclonal antibody (MSB0010718C).

1. Heery CR, et al. J Clin Oncol. 2014;32(Suppl):Abstract 3064; 2. Heery CR, et al. J Clin Oncol 2015;33(Suppl):Abstract 3055; 3. Boyerinas B, et al. Cancer Immunol Res. 2015;May 26 [epub ahead of print]; 4. Gulley JL, et al. J Clin Oncol 2015;33(Suppl):Abstract 8034; 5. Chung HC, et al. Eur J Cancer 2015;51(Suppl S3):Abstract 2364; 6. Disis ML, et al. J Clin Oncol 2015;33(Suppl):Abstract 5509; 7. Apolo AB, et al. Eur J Cancer 2015;51(Suppl S3):Abstract 2630.

Phase Ib cohort expansion



Mn, switch-maintenance; refract, refractory

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Demographics and disease characteristics of patients with TNBC

Characteristics	n=58
Median age, years (range)	52.5 (31.0-80.0)
Gender, n (%)	
Female	58 (100.0)
ECOG PS, n (%)	
0	33 (56.9)
1	25 (43.1)
Subsite of tumor, n (%)	
Ductal	36 (62.1)
Lobular	0
Carcinoma, NOS	6 (10.3)
Other*	16 (27.6)

Characteristics	n=58
# of prior regimens for LA/M disease, excluding (neo-)adjuvant, n (%)†	
≥3	13 (22.4)
2	16 (27.6)
≤1	29 (50.0)
Median time since diagnosis of metastatic disease, months (range)‡	13.2 (0.7, 176.8)

Data cut-off date: February 27, 2015

NOS, not otherwise specified; LA/M, locally advanced/metastatic
* Other denotes patients who were uncoded (11) or other histology (5).
† Regimen for LA/M disease may have included hormonal therapy, either alone or in combination with chemotherapy.
‡ Data on time since diagnosis of metastatic disease was missing for 6 patients.

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Potentially immune-related, treatment-related toxicity

	Treatment-related, potentially immune-related TEAEs, n=168	
	n (%)	grade (n)
Patients with any event	17 (10.1)	Grade 1/2 (13); grade 3/4 (4)
Hypothyroidism	8 (4.8)	Grade 1/2 (8)
Autoimmune hepatitis*	3 (1.8)	Grade 3 (3)
Pneumonitis	3 (1.8)	Grade 1/2 (2); grade 3 (1)
Thrombocytopenia	2 (1.2)	Grade 1 (1); grade 4 (1)

* Autoimmune hepatitis temporarily resolved with steroid treatment, but led to discontinuation in 2 patients; the third patient who experienced autoimmune hepatitis died of acute liver failure in a setting of progressive liver metastasis.

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Antitumor activity of avelumab in patients with MBC

Best overall response*	Overall population (n=168)	Patients with TNBC (n=58)
CR, n (%)	1 (0.6)	0
PR, n (%)	7 (4.2)	5 (8.6)
SD†, n (%)	39 (23.2)	13 (22.4)
PD, n (%)	106 (63.1)	38 (65.5)
Non-evaluable‡, n (%)	15 (8.9)	2 (3.4)
ORR, % (95% CI)	4.8 (2.1, 9.2)	8.6 (2.9, 19.0)
DCR§, %	28.0	31.0

* Unconfirmed best overall response according to RECIST 1.1
† Stable disease at the first post-baseline tumor assessment after 6 weeks was required to qualify for a BOR of SD
‡ Non-evaluable includes 'missing' and 'not assessable'
§ DCR is defined as responses + SD

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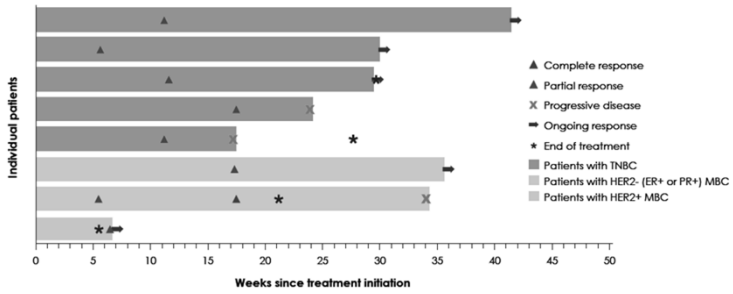
Time to and duration of response



- Median duration of F/U: 10.0 months (range, 6.0-15.2 months)
- Median time to response: 11.4 weeks (range, 5.7-17.7 weeks)
- Median DoR: 28.7 weeks (95% CI: 6.1, ne)
- Responses observed in patients with different molecular subtypes
- Response ongoing in 5/8 patients at time of analysis

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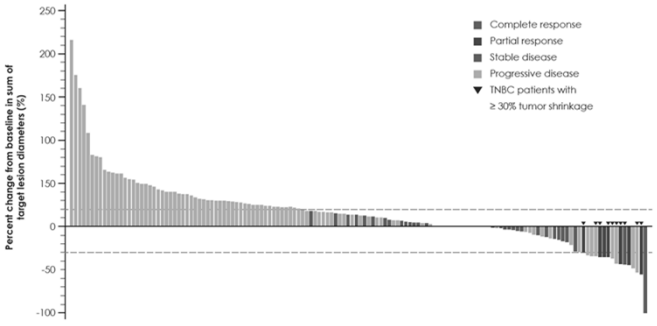
Best change in target lesions from baseline (n=140*)



- Tumor shrinkage by ≥30% was observed in 16 patients (9.5%) in overall MBC population, including 2 patients with PD by RECIST who had PRs by modified irRC
- 17.2% (10/58) of TNBC patients had tumor shrinkage of ≥30%

* Number of patients with baseline tumor assessments and ≥1 post-baseline assessment.

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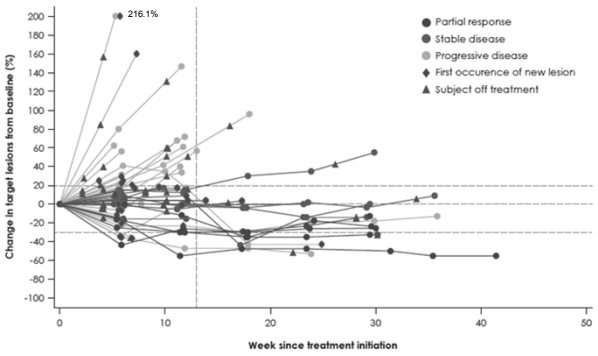
Percent change from baseline in TNBC population (n=46*)



* Number of patients with baseline tumor assessments and ≥1 post-baseline assessment.

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ORR according to molecular subtype

Subtype	n/N1* (%)	95% CI
TNBC	5/58 (8.6)	2.9, 19.0
HER2–/ER+ or PR+	2/72 (2.8)	0.3, 9.7
HER2+	1/26 (3.8)	0.1, 19.6

* N1=total number of patients in subgroup

- Five of 8 responders had TNBC (62.5%)
- Responses also achieved by patients in other subtypes

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PD-L1 expression status according to molecular subtype

PD-L1 expression (total evaluable=136)*	Molecular subtype (evaluable, n)	PD-L1+, n/N1† (%)	PD-L1–, n/N1† (%)
≥1% tumor cells cut-off	TNBC (48)	33/48 (68.8)	15/48 (31.2)
	HER2−/ER+ or PR+ (56)	31/56 (55.4)	25/56 (44.6)
	HER2+ (21)	15/21 (71.4)	6/21 (28.6)
≥5% tumor cells cut-off	TNBC (48)	13/48 (27.1)	35/48 (72.9)
	HER2−/ER+ or PR+ (56)	4/56 (7.1)	52/56 (92.9)
	HER2+ (21)	5/21 (23.8)	16/21 (76.2)
≥25% tumor cells cut-off	TNBC (48)	2/48 (4.2)	46/48 (95.8)
	HER2−/ER+ or PR+ (56)	1/56 (1.8)	55/56 (98.2)
	HER2+ (21)	0/21 (0.0)	21/21 (100.0)
≥10% immune cell "hotspots" cut-off	TNBC (48)	9/48 (18.8)	39/48 (81.2)
	HER2−/ER+ or PR+ (56)	2/56 (3.6)	54/56 (96.4)
	HER2+ (21)	1/21 (4.8)	20/21 (95.2)

* Non-evaluable specimens (n=32) included those that were missing, of poor quality, or otherwise not available to provide results.
† N1=total number of patients in subgroup

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ORR according to PD-L1 expression level in patients evaluable for PD-L1 expression

PD-L1 expression (total evaluable=136)*	PD-L1+, n/N1† (%)	PD-L1–, n/N1† (%)	*p*-value‡
≥1% tumor cells cut-off	3/85 (3.5)	4/51 (7.8)	0.425
≥5% tumor cells cut-off	1/23 (4.3)	6/113 (5.3)	1.000
≥25% tumor cells cut-off	0/3 (0)	7/133 (5.3)	1.000
≥10% immune cell "hotspots" cut-off	4/12 (33.3)	3/124 (2.4)	0.001

* PD-L1 expression status is unknown for the patient who achieved a CR; non-evaluable specimens included those that were missing, of poor quality or quantity (insufficient tissue on slide or insufficient tumor sample), or otherwise not available to provide results; all biopsy or surgical specimens samples were required to be collected within 90 days of first administration of avelumab.
† N1=number of patients with evaluable PD-L1 expression
‡ Fisher's exact test

- PD-L1 expression by immune cells within the tumor ("hotspots") was associated with response to avelumab

ORR according to PD-L1 expression level in TNBC patients evaluable for PD-L1 expression

PD-L1 expression (total evaluable=48)	PD-L1+, n/N1* (%)	PD-L1–, n/N1* (%)
≥1% cut-off	2/33 (6.1)	3/15 (20.0)
≥5% cut-off	1/13 (7.7)	4/35 (11.4)
≥25% cut-off	0/2 (0)	5/46 (10.9)
≥10% immune cell "hotspots" cut-off	4/9 (44.4)	1/39 (2.6)

* N1=number of patients with evaluable PD-L1 expression

- Among patients with TNBC, PD-L1 expression by immune cells within the tumor was associated with response to avelumab
- Among 5 TNBC responders, 4 (80%) had PD-L1+ immune cells

Conclusions

- Avelumab has an acceptable safety profile in patients with MBC
- Despite low ORR in overall unselected MBC cohort, signs of greater clinical activity in specific subsets of patients
  - Among 58 patients with TNBC, 5 (8.6%) had responses to avelumab
  - Patients expressing PD-L1 in immune cells showed higher response rate compared with PD-L1– immune cells (33.3% [4/12] vs 2.4% [3/124])
  - In patients with TNBC, PD-L1 expression by immune cells was associated with clinical response to avelumab (44.4% [4/9] vs 2.6% [1/39])
- Further analysis of PD-L1 expression and clinical activity of avelumab in MBC is ongoing


Thank you !