GBG
GERMAN
BREAST
GROUP

Heilung durch Innovation, Kompetenz und Partnerschaft

Ergebnisse der Translationalen Forschung der GBG - Review of the year

Prof. Dr. Volkmar Müller
Klinik für Gynäkologie, Brustzentrum am UKE
Universitätsklinikum Hamburg-Eppendorf

ASCO ANNUAL MEETING

COLLECTIVE WISDOM

2016

THE FUTURE OF PATIENT-CENTERED CARE AND RESEARCH

June 3-7, 2016

McCormick Place | Chicago, Illinois

#ASCO16

ASCO

ASCO ANNUAL MEETING
COLLECTIVE WISDOM
2016

THE FUTURE OF PATIENT-CENTERED CARE AND RESEARCH

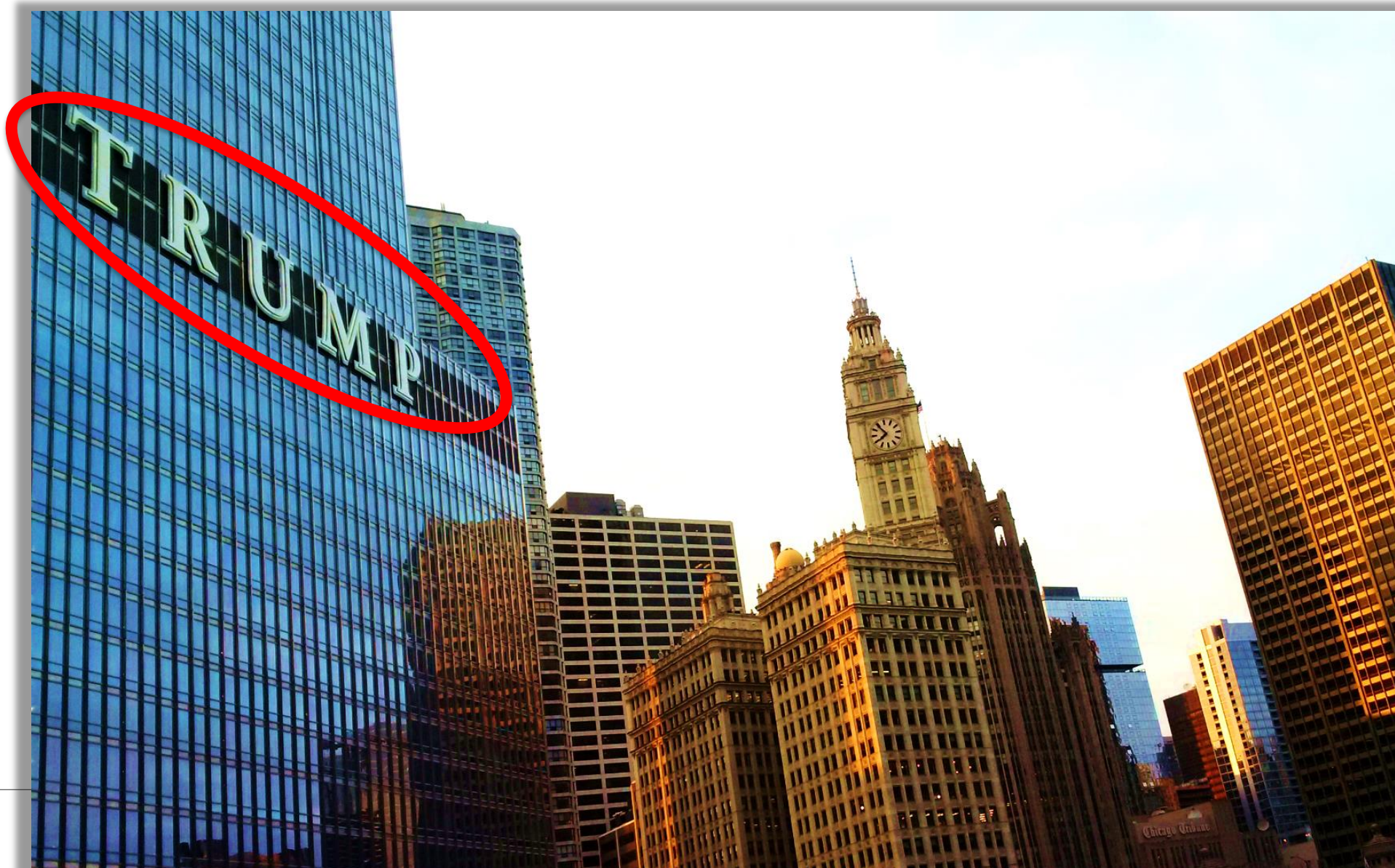
June 3-7, 2016
McCormick Place | Chicago, Illinois
#ASCO16

ASCO®

ASCO ANNUAL MEETING
COLLECTIVE WISDOM
2016
THE FUTURE OF PATIENT-CENTERED CARE AND RESEARCH

June 3-7, 2016
McCormick Place | Chicago, Illinois
#ASCO16

ASCO



ASCO ANNUAL MEETING
COLLECTIVE WISDOM
2016
THE FUTURE OF PATIENT-CENTERED CARE AND RESEARCH

June 3-7, 2016
McCormick Place | Chicago, Illinois
#ASCO16

ASCO

Risk assessment after neoadjuvant chemotherapy in luminal breast cancer – a prospectively planned validation of gene expression based and clinical prognostic scores in 428 residual tumor samples from two neoadjuvant clinical trials

Abstract 522

Carsten Denkert[1], Karsten Weber[2], Kristin Krappmann[3], Jens Huober[4], Frederik Marmé [5], Christian Schem[6], Knut Engels[7], Berit Maria Pfitzner[8], Sherko Kümmel[9], Jenny Furlanetto[2], Arndt Hartmann[10], Silvia Darb-Esfahani[8], Volkmar Müller[11], Annette Staebler[12], Keyur Mehta[2], Gunter von Minckwitz[2], Ralf Kronenwett[3], Sibylle Loibl[2]

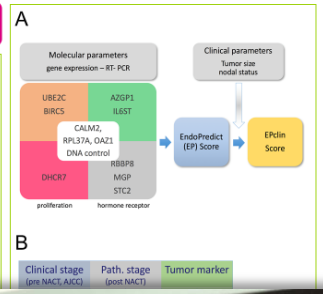
1 Institute of Pathology, Charité - University Hospital and German Cancer Consortium (DKTK), Berlin, Germany; 2 German Breast Group, Neu-Isenburg, Germany.; 3 Sividon Diagnostics, Cologne, Germany ; 4 Department of Gynecology, University Hospital, Ulm; 5 Department of Gynecology and National Tumor Center (NCT), Heidelberg, Germany; 6 Department of Obstetrics and Gynecology, University Schleswig Holstein Campus Kiel; 7 Zentrum für Pathologie, Zytologie und Molekularpathologie Neuss; 8 Institute of Pathology, Charité - University Hospital Berlin, Germany; 9 Breast Cancer Center, Kliniken Essen-Mitte, Essen, Germany 10 Institute of Pathology, University of Erlangen, Germany; 11 Department of Gynecology, Universitätsklinikum Hamburg-Eppendorf, Hamburg, Germany; 12 Institute of Pathology, University of Tübingen, Germany

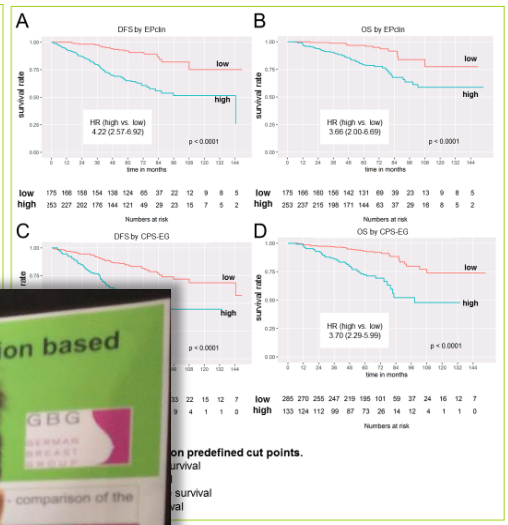
Background

Gene expression assays are well-established prognostic tools for planning of adjuvant therapy in luminal breast cancer (BC). In the neoadjuvant setting, pCR is not an optimal prognostic factor in luminal BC, and additional parameters are needed.

Aims of the study:

1) Evaluation of the gene expression test EndoPredict (EP and EPclin) performed on residual tumor specimen after NACT for predicting prognosis in patients (pts) with ER+/HER2- BC who did not achieve a pCR and
2) Comparison of its prognostic power with the CPS-EG score





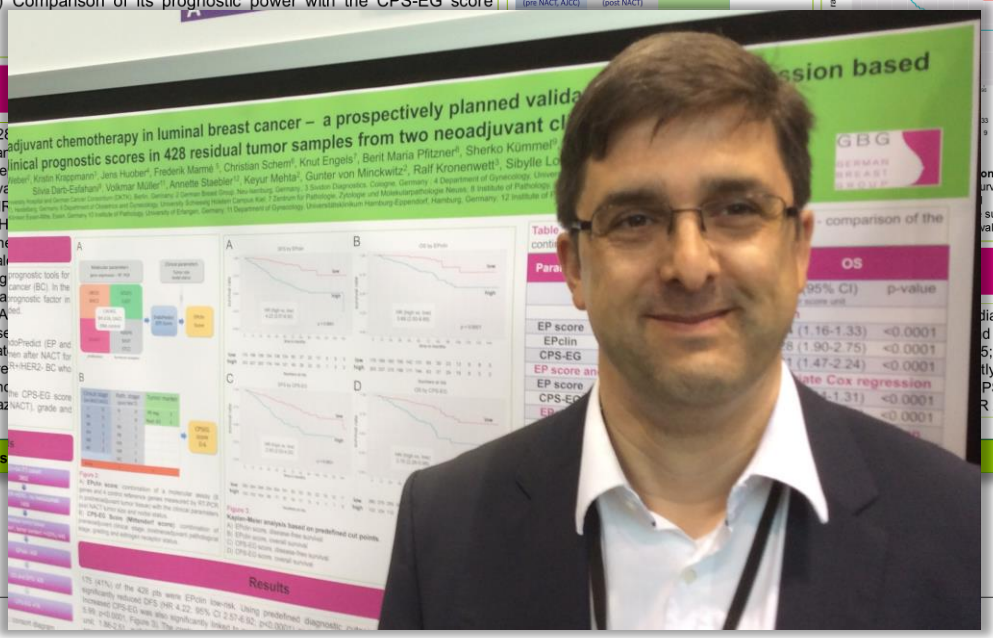


Table 1: Univariate and multivariate Cox regression - comparison of the continuous EP, EPclin and CPS-EG scores

Parameter	DFS		OS	
	HR (95% CI) per score unit	p-value	HR (95% CI) per score unit	p-value
Univariate Cox regression				
EP score	1.22 (1.16-1.29)	<0.0001	1.24 (1.16-1.33)	<0.0001
EPclin	2.16 (1.86-2.51)	<0.0001	2.28 (1.90-2.75)	<0.0001
CPS-EG	1.70 (1.43-2.02)	<0.0001	1.81 (1.47-2.24)	<0.0001
EP score and CPS-EG score - combined bivariate Cox regression				
EP score	1.20 (1.13-1.27)	<0.0001	1.22 (1.14-1.31)	<0.0001
CPS-EG	1.57 (1.32-1.86)	<0.0001	1.67 (1.35-2.06)	<0.0001
EPclin and CPS-EG score - combined bivariate Cox regression				
EPclin	2.09 (1.73-2.53)	<0.0001	2.16 (1.72-2.72)	<0.0001
CPS-EG	1.06 (0.85-1-31)	0.61	1.12 (0.86-1.46)	0.39

Conclusions

In this prospectively planned biomarker study we show that the information in the hybrid clinico-molecular EPclin score is also prognostic for DFS and OS after NACT. EPclin provides additional prognostic information to CPS-EG. This approach can be used to assess prognosis after NACT in the luminal non-pCR patient population, and select patients for post-NACT therapies, e.g. treatment with CDK4/6 inhibitors. An additional prospective validation is planned in the ongoing Penelope B trial.

References

1. Filipits M, et al. A new molecular predictor of distant recurrence in ER-positive, HER2-negative breast cancer adds independent information to conventional clinical risk factors. Clin Cancer Res.2011 Sep 15;17(18):6012-20.
2. Mittendorf EA, et al. Validation of a novel staging system for disease-specific survival in patients with breast cancer treated with neoadjuvant chemotherapy. J Clin Oncol. 2011 May20;29(15):1956-62.
3. Marmé F. Utility of the CPS+EG staging system in hormone receptor-positive, human epidermal growth factor receptor 2-negative breast cancer treated with neoadjuvant chemotherapy. Eur J Cancer. 2016 Jan;53:65-74.

This study has been funded by the Translational Oncology programme of the German Cancer Aid ("Deutsche Krebshilfe") within the Project TransLUMINAL-B.

Deutsche Krebshilfe
HELFEN. FORSCHEN. INFORMIEREN.

GBG
GERMAN
BREAST
GROUP

Kann ein Genexpressionstest zusätzliche Informationen nach neoadjuvanter Chemotherapie bei Hormonrezeptor-positiven Patientinnen liefern?

Aims of the study:

1) **Evaluation of the gene expression test EndoPredict (EP and EPclin) performed on residual tumor specimen after NACT for predicting prognosis in patients (pts) with ER+/HER2- BC who did not achieve a pCR.**

2) **Comparison of its prognostic power with the CPS-EG score that combines tumor stage (pre- and post NACT), grade and ER status.**

Vergleich Endopredict am OP-Präparat mit dem CPS-EG Score

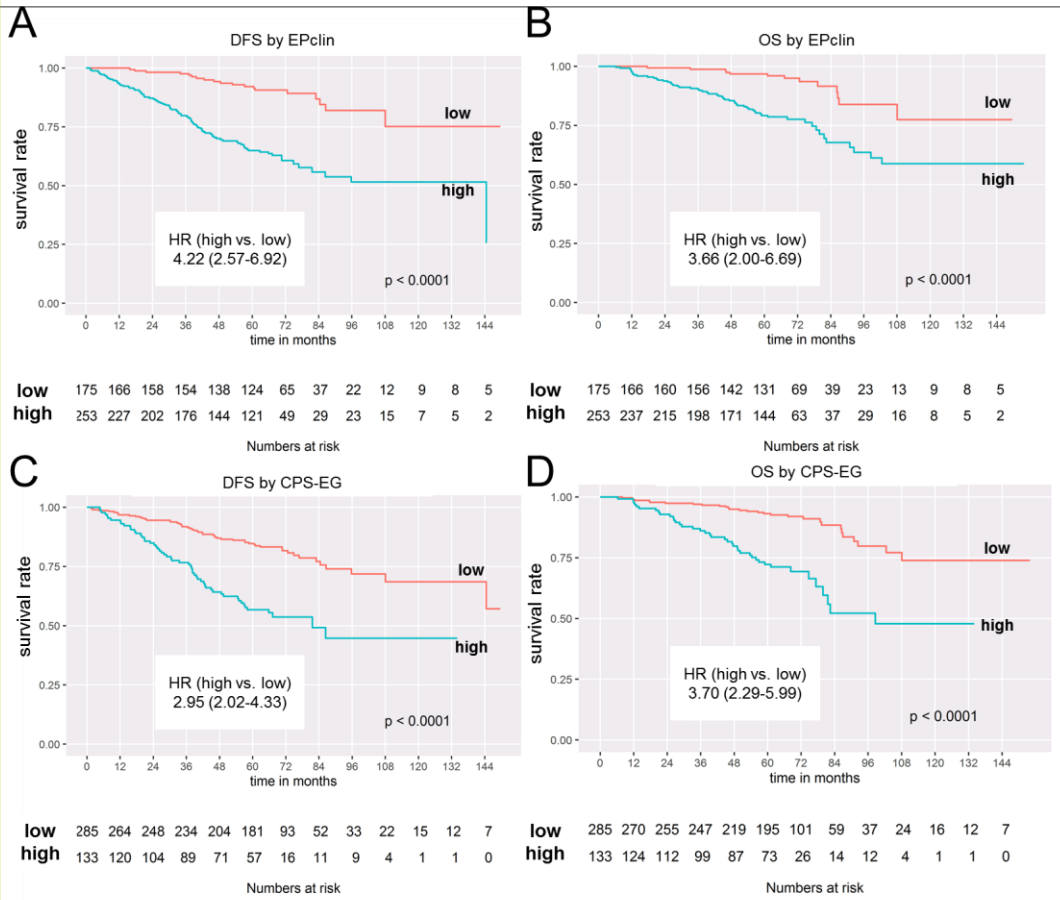


Figure 3:

Kaplan-Meier analysis based on predefined cut points.

A) EPclin score, disease-free survival
B) EPclin score, overall survival
C) CPS-EG score, disease-free survival
D) CPS-EG score. overall survival

GBG
GERMAN
BREAST
GROUP

Schlussfolgerung

- In this prospectively planned biomarker study we show that the information in the hybrid clinico-molecular EPclin score is also prognostic for DFS and OS after NACT.
- EPclin provides additional prognostic information to CPS-EG.
- This approach can be used to assess prognosis after NACT in the luminal non-pCR patient population, and select patients for post-NACT therapies, e.g. treatment with CDK4/6 inhibitors.

Endopredict am OP-Präparat liefert zusätzliche Informationen zu CPS-EG Score -> wichtig für postneoadjuvante Studien

GBG
GERMAN
BREAST
GROUP

Dezember: Auf nach San Antonio

GBG
GERMAN
BREAST
GROUP

SAN ANTONIO
BREAST CANCER
SYMPOSIUM®

Comparison of the mutational landscape of breast cancer during pregnancy and non-pregnant controls

Sibylle Loibl[1], Nicole Pfarr[2], Karsten Weber[1], Tanja Neunhöffer[3] Sonia Villegas[4], Albrecht Stenzinger[5], Jenny Furlanetto[1], Bahriye Aktas[6], Jan Budczies[4], Frederik Marmé[7], Laura Kahmann[8], Carsten Denkert[4], Wilko Weichert[2]

[1]German Breast Group; Neu-Isenburg, Germany, [2]Institute of Pathology, Technical University Munich, Germany, [3]Departement of Gynaecology, Helios Clinics Wiesbaden, Germany, [4]Institute of Pathology, Charité Berlin, Berlin, [5]Institute of Pathology, University Hospital Heidelberg, [6]University Women´s Hospital, Essen, [7]NCT, Section Translational Gynaecologic Oncology, Heidelberg, [8]Clinic Landkreis Neumarkt, Parsberg, Germany

P1-03-09

Background

Breast cancer during pregnancy (BCP) is a rare coexistence and is associated with contradicting results about its biology and prognosis[1,2]. Little is known about the impact of pregnancy on breast cancer biology at the genomic level. Based mainly on classical immunohistochemistry and mutational analysis in one small dataset[3,4] it is believed that BCP during pregnancy is biologically not different from breast cancer diagnosed outside pregnancy.

The aim of the study is to compare the pattern of somatic mutations between pregnant and non-pregnant patients with breast cancer using a dataset of pregnant patients enrolled in BCP study and non-pregnant controls obtained from TCGA database.

Materials and Methods

The BCP study (GBG 29; BIG 03-02) is a multicenter observational study for breast cancer during pregnancy. Formalin-fixed paraffin embedded (FFPE) core biopsies taken before therapy were retrospectively analysed for somatic mutations using an Ion Torrent: Proton/PGM sequencing platform (Figure 1). The samples were assayed on a custom designed Breast Cancer Panel (BCPv2)[5] that comprises 236 amplicons split into two primer pools and covers hotspot regions of 138 exons of 25 genes (Table 1). Raw data analyses were performed using the Ion Torrent Suite Software (version 4.4). Only non-synonymous mutations that have not been reported as being of germline origin were processed further. All statistical tests were by default 2-sided, significance level was set to α=0.05.

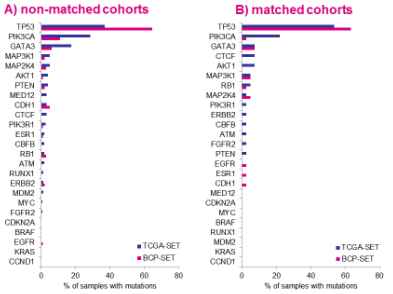
Results

Table 2. Clinical characteristics in BCP vs. non-pregnant controls

		non-matched		matched	
Parameter	Category	BCP-cohort	TCGA-cohort	BCP-cohort	TCGA-cohort
Age, years	median	34	40	37	38
	min-max	26-43	26-45	28-43	26-45
Tumor size	T1-2	82 (82.8%)	130 (85.0%)	37 (90.2%)	34 (82.9%)
	T3-4	17 (17.2%)	23 (15.0%)	4 (9.8%)	7 (17.1%)
Nodal status	negative	48 (49.5%)	61 (39.6%)	23 (57.5%)	14 (34.1%)
	positive	49 (50.5%)	93 (60.4%)	17 (42.5%)	27 (65.9%)
Grading*	G1-2	30 (30.3%)	52 (49.5%)	12 (29.3%)	
	G3	69 (69.7%)	53 (50.5%)	29 (70.7%)	
HR*	positive	43 (43.4%)	104 (72.2%)	21 (51.2%)	
	negative	56 (56.6%)	40 (27.8%)	20 (48.8%)	
HER2*	positive	13 (13.1%)	24 (16.2%)	1 (2.4%)	
	negative	86 (86.9%)	124 (83.8%)	40 (97.6%)	

*Numbers in matched BCP-set vs.TCGA-set are identical by definition of the matching

Figure 2. Mutation patterns overall in BCP vs. non-pregnant controls

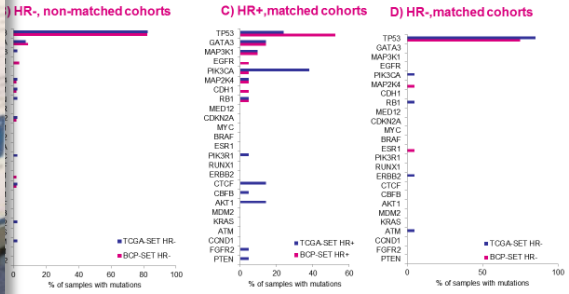


- Comparison of the mutational patterns between BCP and non-pregnant controls (TCGA cohort) before any matching showed overall 102 mutations (average 1.03 mutations per samples) in BCP dataset vs. 195 (average 1.27 mutations per sample) in the TCGA. The most frequent somatic mutations for both cohorts were detected in *TP53* (65% vs. 37%), *PIK3CA* (11% vs. 29%) and *GATA3* (6% vs. 18%; Figure 2).
- Exact matching (1:1) in BCP and TCGA cohorts was performed based on age (26-30 vs. 31-35 vs. 36-40 vs. 41-45), HR (positive vs. negative), HER2 (positive vs. negative) and grading (G1/2 vs. G3) and yielded 41 patients from both datasets (Table 2).
- In the matched cohorts BCP patients had significantly less frequently N+ tumors as compared to non-pregnant controls (p=0.046) with no significant difference for *TP53* (p=0.502) and *GATA3* (p=1.000) mutational status whereas *PIK3CA* mutations were detected in only 2.4% of the pregnant patients vs. 22.0% of the non-pregnant controls (p=0.015; Figure 2). Within HR subgroups, overall *TP53* was the most frequently mutated gene with higher mutational rate in HR-negative subgroup (52.4% vs. 75.0% for BCP; 23.8% vs. 85.0% for TCGA control; Figure 3).

Table 1.

Genes
GATA3
PTEN
FGFR2
CCND1
ATM
KRAS
MDM2
RB1
AKT1
CBFB
CTCF
CDH1
TP53
MAP2K4
ERBB2
RUNX1
PIK3CA
MAP3K1
PIK3R1
ESR1
EGFR
BRAF
MYC
CDKN2A
MED12
25 Genes

R status in BCP vs. non-pregnant controls



Conclusions

Overall the mutational landscape does not seem to be different between pregnant patients and no-pregnant controls The imbalances in *PIK3CA* mutational rate after matching might be explained by a remaining bias caused by differences in sensitivity or specificity of methods used to detect mutations or differences in variables not used for matching. Further comparisons using other datasets, looking into gene expression patterns are currently conducted.

References

1.Azim HA Jr, Botteri E, Renne G et al. The biological features and prognosis of breast cancer diagnosed during pregnancy: a case-control study. Acta Oncol. 2012; ;51(5):653-61.
2.Amant F, von Minckwitz G, Han SN, et al. Prognosis of women with primary breast cancer diagnosed during pregnancy: results from an international collaborative study. J Clin Oncol. 2013 10;31(20):2532-9.
3.Azim HA Jr, Brohée S, Peccatori FA et al. Biology of breast cancer during pregnancy using genomic profiling. Endocr Relat Cancer. 2014;21(4):545-54.
4.Loibl S, Han SN, Amant F. Being Pregnant and Diagnosed with Breast Cancer.
Breast Care (Basel). 2012;7(3):204-209
5. Pfarr N, Penzel R, Endris V et al. Targeted next-generation sequencing enables reliable detection of HER2 (ERBB2) status in breast cancer and provides ancillary information of clinical relevance. Genes Chromosomes Cancer. 2016;doi: 10.1002/gcc.22431[Epub]

Presented

German Cancer Consortium (DKTK) and the BANSS Foundation.

GBG
GERMAN
BREAST
GROUP

Ziel

- The aim of the study is to compare the pattern of somatic mutations between pregnant and non-pregnant patients with breast cancer using a dataset of pregnant patients enrolled in BCP study and non-pregnant controls obtained from TCGA database

Gibt es genetische Unterschiede im Tumor zwischen Mammakarzinomen innerhalb und außerhalb der Schwangerschaft?

GBG
GERMAN
BREAST
GROUP

Schlussfolgerung

- **Conclusion: Overall the mutational landscape does not seem to be different between pregnant patients and no-pregnant controls**

Nein!

GBG
GERMAN
BREAST
GROUP

Neoadjuvante Therapie

HRD-Defizit als prädiktiver Faktor für das Ansprechen aus Carboplatin?

Homologous recombination deficiency (HRD) score as a measure to predict the effect of carboplatin on survival in the neoadjuvant phase II GeparSixto trial in triple-negative early breast cancer

Gunter von Minckwitz[1], Kirsten Timms[2], Michael Untch[3], Eric Hahnen[4], Peter A. Fasching[5], Andreas Schneeweiss[6], Christoph T. Salat[7], Mahdi Rezai[8], Jens U. Blohmer[9], Dirk M. Zahm[10], Christian Jackisch[11], Bernd Gerber[12], Peter Klare[13], Sherko Kümmel[14], Stefan Paepke[15], Rita Schmutzler[4], Suzanna Chau[2], Julia Reid[2], Valentina Nekljudova[1], Karsten E. Weber[1], Sibylle Loibl[1,16] for the GBG/AGO-B study groups

[1]German Breast Group, Neu-Isenburg, Germany, [2]Myriad, [3]Department of Obstetrics and Gynecology, Helios Clinics Berlin-Buch, Germany, [4]Center for Hereditary Breast and Ovarian Cancer, Center for Integrated Oncology (CIO), University Hospital Cologne, Cologne, Germany, [5]University Women's Hospital Erlangen, Germany, [6]University Women's Hospital Heidelberg; Germany, [7]Medical Center for Hematology and Oncology Munich MVZ GmbH, Munich, Germany, [8]Department of Gynecology, Luisenkrankenhaus GmbH, Düsseldorf, Germany, [9]Charité, Breast Center, Berlin, Germany, [10]Women's Hospital, SRH Wald-Clinic Gera, Germany, [11]Women's Hospital Offenbach, Germany, [12]University Women's Hospital Rostock, Germany, [13]Praxisklinik, Berlin; Germany, [14]Breast Center Clinics Essen-Mitte, Essen, Germany, [15]TU Munich, Munich, Germany, [16]Center for Hematology and Oncology Bethanien-Hospital, Frankfurt am Main, Germany

P 1-09-02

Background & Aim

Homologous recombination–deficient (HRD) tumors have lost the ability to repair double-stranded DNA breaks, resulting in increased susceptibility to DNA-damaging drugs such as platinum agents. Genomic instability and a high frequency of g*BRCA1* and g*BRCA2* mutations are commonly associated with triple-negative breast cancer (TNBC)[1]. Addition of carboplatin to anthracycline/taxane-based neoadjuvant chemotherapy has been shown to increase pathological complete response (pCR; ypT0 ypN0) rates in patients with TNBC in two large phase II studies (GeparSixto[2] and CALGB 40603[3]).

Patients with HRD tumors and those with a g*BRCA*, had in general a higher pCR rate with and without carboplatin[1]. Patients with pCR had in general a better prognosis, irrespective of the g*BRCA* status.

To determine whether HRD can predict the effect of carboplatin on survival in TNBC subgroup from GeparSixto trial, we corre

Gepa
pros
desi
para
cent
asse
(tmB
scor
scor
imba
scor
dele
intac
defic
muta

Stat
The
exac
a pr
meth

Results

Figure 1. Study design for the TNBC subgroup

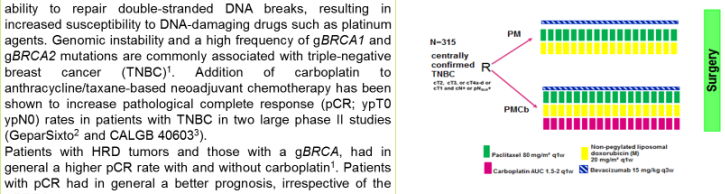


Figure 2. Overlap of HRD & *BRCA* mutations

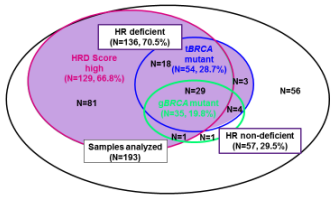


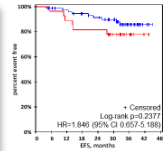
Table 1. Multivariate model for EFS

Predictor	Value	HR	95 % CI	p-value
HRD	yes vs. no	0.632	0.333-1.201	0.1662
Arm	PMCb vs. PM	0.478	0.253-0.905	**0.0202**
age	≥ 50 vs. <50	0.576	0.292-1.139	0.1052
cT	cT2-4 vs. cT1	2.507	0.880-7.144	0.0538
cN	N+ vs. N0	2.483	1.301-4.740	**0.0048**
Grading	G3 vs. G1-2	1.088	0.535-2.214	0.8151
Ki67	≥ 60% vs. <60%	1.208	0.578-2.523	0.6116
LPBC	yes vs. no	0.376	0.146-0.967	**0.0231**

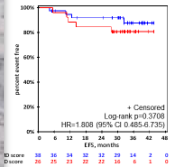
Figure 3. EFS by HR-deficiency & according to treatment

A) by HRD status

B) by HRD in PM arm



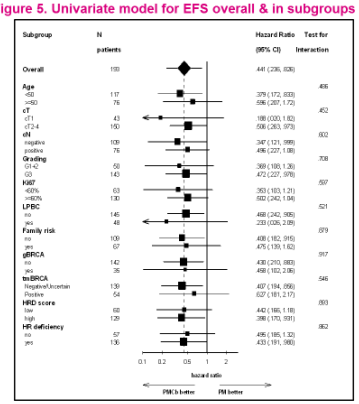
C) by HRD in PMCb arm



& according to treatment

) tm*BRCA* intact tumors+PMCb

Figure 5. Univariate model for EFS overall & in subgroups



- After median follow-up of 34.3 months for EFS, 43 events have been reported.
- Overall, patients with HR-deficient tumors showed a better EFS than HR-non-deficient ones (p=0.0526, Figure 3).
- Patients with HRD high score and *BRCA* intact tumors had better but not statistically significant EFS rates as compared to HR-non-deficient patients (p=0.2223, Figure 4).
- HR-deficiency did not predict the effect of carboplatin on EFS (Figure 5).
- The multivariate analysis revealed that the therapy (p=0.0202), clinical nodal status before treatment (p=0.0048), and lymphocyte predominant breast cancer (LPBC; p=0.0231) but not HRD (p=0.1662) were independent significant prognostic factors for EFS (Table 1).

Conclusions

Within the GeparSixto study the HR-deficiency (either HRD score high or *BRCA* mutation) was in general associated with a higher pCR rate and an improved EFS. The effect on EFS of adding carboplatin could not be predicted by the HRD score in this underpowered study. However, the results can help to understand the role of HR-deficiency and the value of the HRD score in TNBC especially in patients without *BRCA* mutation. Nodal status and LPBC remained the strongest prognostic factors along with Carboplatin therapy.

References

1. von Minckwitz G, Hahnen E, Fasching PA, et al. Pathological complete response (pCR) rates after carboplatin-containing neoadjuvant chemotherapy in patients with germline BRCA (gBRCA) mutation and triple-negative breast cancer (TNBC): Results from GeparSixto (ASCO 2014).
2. von Minckwitz G, Schneeweiss A, Loibl S, et al. Neoadjuvant carboplatin in patients with triple-negative and HER2-positive early breast cancer (GeparSixto; GBG 66): a randomised phase 2 trial. Lancet Oncol. 2014;15(7):747-56.
3. Sikov WM, Berry DA, Perou CM, et al. Impact of the addition of carboplatin and/or bevacizumab to neoadjuvant once-per-week paclitaxel followed by dose-dense doxorubicin and cyclophosphamide on pathologic complete response rates in stage II to III triple-negative breast cancer: CALGB 40603 (Alliance). J Clin Oncol. 2015;33(1):13-21.

upported by Myriad and Teva

GBG
GERMAN
BREAST
GROUP

HRD in Geparsixto: Fragestellung

- To determine whether HRD can predict the effect of carboplatin on survival in TNBC subgroup from GeparSixto trial, we correlated the HRD status to the event free survival (EFS).

Kann ein Defizit in der der homologen DNA-Reparatur (HRD) ein besseres Ansprechen auf Carboplatin vorhersagen?

GBG
GERMAN
BREAST
GROUP

HRD in Geparsixto: Schlussfolgerung

- Within the GeparSixto study the HR-deficiency (either HRD score high or *BRCA* mutation) was in general associated with a higher pCR rate and an improved EFS.
- The effect on EFS of adding carboplatin could not be predicted by the HRD score in this underpowered study.
- However, the results can help to understand the role of HR-deficiency and the value of the HRD score in TNBC especially in patients without *BRCA* mutation.

Defizit in der der homologen DNA-Reparatur (hoher HRD-Score oder BRCA-Mutation) höhere pCR-Rate und besseres Rezidivfreies Überleben, aber bessere Wirksamkeit von Carbo lässt sich nicht vorhersagen

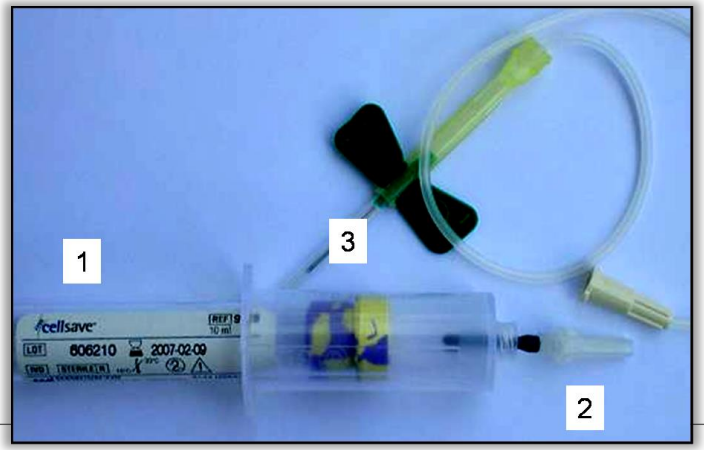
GBG
GERMAN
BREAST
GROUP

Rolle zirkulierender Tumorzellen bei neoadjuvanter Therapie

Projektvorschlag 2005

Monitoring of tumor cells in the blood of breast cancer patients treated with neoadjuvant chemotherapy: Examining a potential surrogate marker for clinical response to therapy

Universitätsklinikum Hamburg-Eppendorf



GBG
GERMAN
BREAST
GROUP

Rolle zirkulierender Tumorzellen bei neoadjuvanter Therapie

Projektvorschlag 2005

Monitoring of tumor cells in the blood of breast cancer patients treated with neoadjuvant chemotherapy: Examining a potential surrogate marker for clinical response to therapy

Universitätsklinikum Hamburg-Eppendorf

Published OnlineFirst April 20, 2010; DOI: 10.1158/1078-0432.CCR-09-2042

Imaging, Diagnosis, Prognosis

Clinical Cancer Research

Detection and HER2 Expression of Circulating Tumor Cells: Prospective Monitoring in Breast Cancer Patients Treated in the Neoadjuvant GeparQuattro Trial

Sabine Riethdorf[1], Volkmar Müller[2], Liling Zhang[1], Thomas Rau[3], Sibylle Loibl[4,5], Martina Komor[4], Marc Roller[4], Jens Huober[6], Tanja Fehm[6], Iris Schrader[7], Jörn Hilfrich[7], Frank Holms[8], Hans Te... Holger Eidtmann[10], Michael Untch[11], Gunter von Minckwitz[4], and Klaus Pantel[1]

Erste Publikation 2010

Rolle zirkulierender Tumorzellen bei neoadjuvanter Therapie

San Antonio Breast Cancer Symposium – December 6-10, 2016

institutCurie

International MEta-analysis of circulating tumor cell detection in early breast cancer pts treated by NEOadjuvant chemotherapy (IMENEO study)

FC Bidard*, S Michiels, V Mueller, S Riethdorf, LJ Esserman, A Lucci, B N
R Gisbert-Criado, S Sleijfer, M Toi, JA Garcia-Saenz, A Hartkopf, D Gener
J Smerage, L Muinelo, J Stebbing, P Viens, M Magbanua, CS Hall, O Eng
J Vidal-Martínez, W Onstenk, N Fujisawa, E Diaz-Rubio, FA Taran, MR C
M Ignatiadis, C Proudhon, D Wolf, J Bowman Bauldry, E Borgen, R Naga
J Kraan, M Maestro, SY Brucker, K Weber, F Reyal, D Amara, MG Karhad
H Tokiniwa, A Llombart-Cussac, K d'Hollander, P Cottu, JW Park, S Loibl,

* Medical Oncology, Institut Curie, Paris, France

Data collection

Letter of intent

#2,000 potentially eligible pts from 18 centers

call for data → 2 centers off study

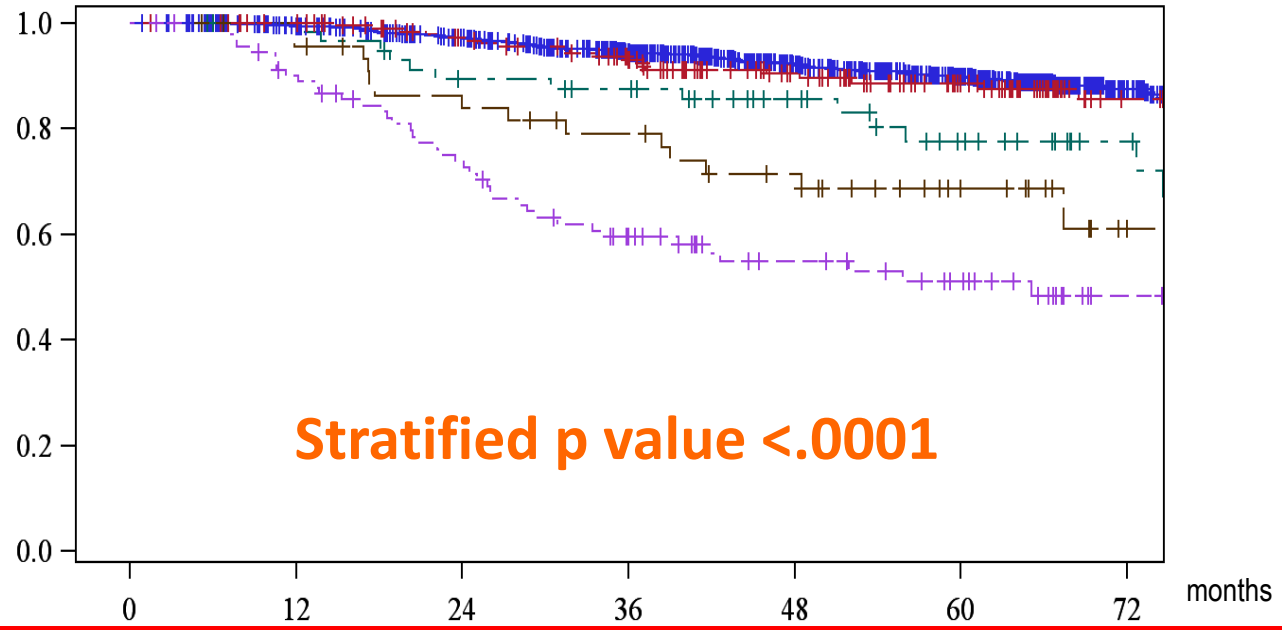
2,239 pts data received

data cleaning → 83 excluded

2,156 individual patients
21 studies
16 centers

746 Patientinnen aus GBG-Studien!

CTC before NCT & Overall Survival



Kürzeres Gesamtüberleben bei Nachweis von Tumorzellen im Blut vor neoadjuvanter Chemotherapie

	N pts	% events	Hazard Ratio
0 CTC	1175	9.8%	1
1 CTC	199	10.6%	1.09 [0.65-1.69]
2 CTC	59	23.7%	**2.63** [1.42-4.54]
3-4 CTC	47	29.8%	**3.84** [2.08-6.66]
≥ 5 CTC	93	46.2%	**6.25** [4.34-9.09]

Overall clinical validity (single point; ≥2 CTC)

institutCurie
Together, let's beat cancer.

Multivariate analyses

Time point	OS		DDFS		LRFI	
	HR	p	HR	p	HR	p
CTC at baseline *(landmark analysis)*	4.19 [2.97-5.88]	<.0001	3.79 [2.84-5.03]	<.0001	3.20 [1.93-5.19]	<.0001
CTC [-5;0]w before surgery *(landmark analysis)*	2.56 [1.45-4.23]	.0020	2.69 [1.67-4.12]	<.0001	1.05 [0.32-2.55]	.92

Nachweis von Tumorzellen im Blut vor neoadjuvanter Chemotherapie unabhängiger und zusätzlicher Prognosefaktor

Evaluation of tumor-infiltrating lymphocytes (TILs) as predictive and prognostic biomarker in different subtypes of breast cancer treated with neoadjuvant therapy - a metaanalysis of 3771 patients

Carsten Denkert, Gunter von Minckwitz, Silvia Darb-Esfahani, Barbara Ingold-Heppner, Frederick Klauschen, Jenny Furlanetto, Berit Pfitzner, Jens Huober, Wolfgang Schmitt, Jens-Uwe Blohmer, Sherko Kümmel, Knut Engels, Bianca Lederer, Andreas Schneeweiss, Arndt Hartmann, Christian Jackisch, Michael Untch, Claus Hanusch, Karsten Weber, Sibylle Loibl

GBG

GERMAN
BREAST
GROUP

Fazit

- **Auch im letzten Jahr starke Präsenz translationaler Forschung der GBG auf internationalen Kongressen**

Verdienst vieler Beteiligter:

- Ärzte
- Pflege
- Studienteams
- Patientinnen

GBG
GERMAN
BREAST
GROUP

HERZLICHEN DANK!

GBG Subboard Translationale Forschung