"An **international scientific symposium** for interaction and exchange among basic scientists and clinicians in breast cancer."

40 YEAR ANNIVERSARY

HIGHLIGHTS FROM SAN ANTONIO BREAST CANCER SYMPOSIUM®

2017 DEC. 5-9

Henry B. Gonzalez Convention Center, San Antonio, Texas, USA

UT Health San Antonio

AACR American Association for Cancer Research

Baylor College of Medicine

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SAN ANTONIO BREAST CANCER SYMPOSIUM®

Dear Colleagues,

Thank you for submitting your work and for participating in the 40th annual San Antonio Breast Cancer Symposium. This year, we were happy to celebrate 40 years of connecting people from all over the world with the common goal of advancing scientific knowledge of breast cancer and discovering novel therapies. New to this year's conference were two Tuesday morning workshops: one focused on the molecular biology of breast oncology and the other on methods of breast cancer research. Also new was the introduction of a debate style review of a controversial topic. These sessions were well received and will be included again in future programs.

Now that we have passed the milestone of our 40th symposium, we look forward to a wonderful conference next December 2018. We hope to continue to innovate and adjust along with this dynamic field of cancer research and treatment, and new sessions will be added to the program next year. In this report, you will find highlighted some of the research and trials presented this year with audio and video links. We hope you find this a useful reference when reviewing the major presentations of the conference.

On behalf of the executive committee, we hope you enjoyed your week in San Antonio and look forward to seeing you next December for the 41st annual San Antonio Breast Cancer Symposium.

Sincerely,

Kate Lathrop, MD

40 YEAR ANNIVERSARY

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CONTENT

Basic science/translational research

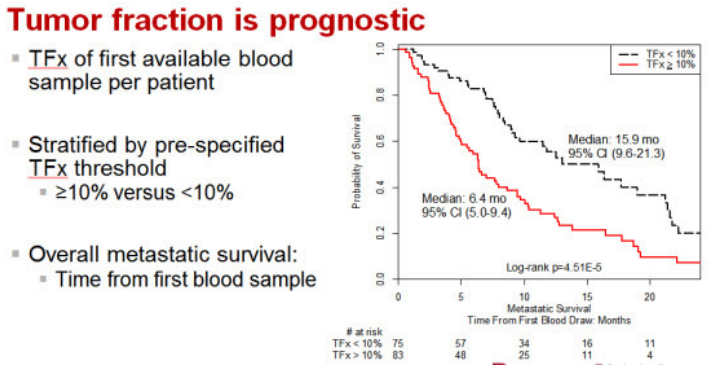
[GS3-07] Genome-wide copy number analysis of chemotherapy-resistant metastatic triple-negative breast cancer from cell-free DNA

Triple negative breast cancer (TNBC) is an aggressive subtype of breast cancer with relatively few somatic mutation with an average of about seven driver mutations per patient. However, there is often extensive somatic copy number alterations (SCNA) with the majority of primary TNBC having at least 50% of the genome altered. Cell free DNA (cfDNA) is DNA that is released into the circulation by cells, both cancerous and non-cancerous. Cell free DNA has potential use as a method of gathering genomic information without a tissue biopsy and for tracking patient-specific mutations. There is also interest in using cell free DNA in genomic discovery research. A new method of ultra-low pass whole genome sequencing (ULP-WGS) is being utilized to identify somatic copy number alternations, and from this calculate the "tumor fraction" of cfDNA. A tumor fraction of at least 10% is sufficient to identify somatic copy number alterations. The benefits of this method are that it is relatively inexpensive and it does not require tumor or germline sequencing data. It is also optimal for tumors like TNBC with extensive somatic copy number alternations.

Dr. Stover presented a study of genome-wide copy number analysis of cell free DNA in patients with chemotherapy resistant metastatic TNBC. The primary objective was to evaluate the association of cfDNA tumor fraction and copy number alterations with time of survival in patients with metastatic TNBC. The group hypothesized that specific SCNAs are more frequent in chemoresistant metastatic TNBCs compared to chemotherapy naïve primary TNBC. They also hypothesized that the cell free DNA tumor fraction of 10% or greater would be associated with a worse overall survival in metastatic TNBC.

The investigators identified 164 patients at the Dana Farber Cancer Center with biopsy proven metastatic TNBC who had previously received chemotherapy. Of these patients, a sample size of 101 patients had at least one sample with a tumor fraction over 10% and 57 patients with no samples containing a tumor fracture over 10%. The patient and tumor characteristics were similar in the two groups. (Insert Slide 7 here)

The authors found that most patients with metastatic TNBC have detectable tumor derived circulating DNA, and that genome wide evaluation via cfDNA is feasible. Also, primary and metastatic TNBC have similar copy numbers with certain regions being altered more commonly in the metastatic setting. Tumor fraction of 10% or more is associated with decreased survival even with control for other clinical and pathologic features. Potential clinical applications of this new technology include using tumor fraction of cfDNA as a prognostic biomarker and evaluating the change in tumor fraction as a predictive biomarker in response to therapy.



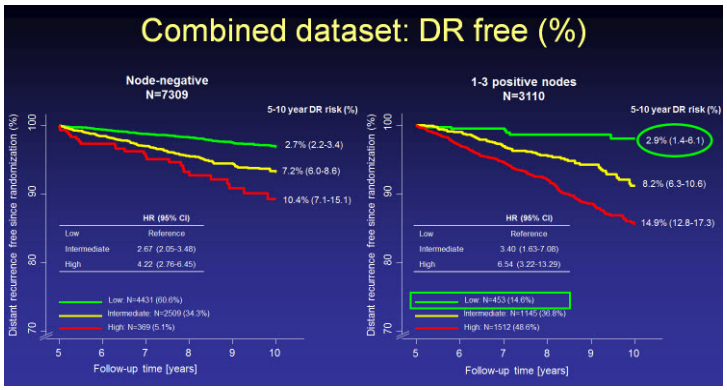
To Hear Content from the Audio Clip Section of the Presentation **GS3-07** CLICK HERE

[GS6-01] Integration of clinical variables for the prediction of late distant recurrence in patients with estrogen receptor positive breast cancer treated with 5 years of endocrine therapy.

Estrogen receptor positive breast cancer is the most common subtype of breast cancer and risk of recurrence after initial treatment is significant with recurrence ranging between 10-40% depending on stage and tumor biology. Extended endocrine therapy can decrease the risk of recurrence for some patients, but there continues to be questions regarding the optimal duration of hormonal therapy. Thus, the ability to accurately predict the probability of distant recurrence after five year of hormonal therapy is an important clinical question. The primary aims of this study presented by Dr. Sestak were to develop and validate a prognostic tool (CTS5) to predict late distant recurrence using standard clinicopathological parameters, and to compare prognostic performance of CTS5 to the published Clinical Treatment Score (CTS0). The CTS0 was developed with clinical trial data from TransATAC in women with available IHC data and who did not receive chemotherapy.

This study included postmenopausal women with estrogen receptor positive breast cancer who had no evidence of recurrence after 5 years of endocrine therapy. Previous chemotherapy was permitted. The primary endpoint was disease free recurrence after 5 years of endocrine therapy. The model divided patients into three groups: Low (less than 5% disease recurrence 5-10 years), intermediate (5-10% disease recurrence 5-10 years) and high (>10% disease recurrence 5-10 years). The main ATAC trial was the training data set for the model with the inclusion of 4,735 patients from this trial. All were postmenopausal women with estrogen receptor positive breast cancer who received 5 years of either tamoxifen or anastrozole. Women with incomplete data or recurrence within the first five years were excluded from the data set. The BIG1-98 trial served as the validation data set and this data set included 6,711 postmenopausal women with estrogen receptor positive breast cancer. The BIG1-98 trial included women treated with either 5 years of tamoxifen, 5 years of letrozole or 2 years of tamoxifen followed by 3 years

of letrozole. Again, women with missing data or recurrent disease within the first 5 years from diagnosis were excluded from the data set. The final CTS5 model included 5 groups for nodal status, a continuous term for tumor size, the three standard groups for grade, and a continuous term for age. The authors reported that this model outperformed the CTS0 model and was highly prognostic for prediction of late distant recurrence. The CTS5 model identified a larger proportion (42%) of women at low risk for recurrence where extended hormonal therapy would be of low benefit. Strengths of this model are the use of common clinicopathologic parameters which are available in virtually all breast cancer patients, and the model included women previously treated with chemotherapy. Of note, the model is applicable to postmenopausal women only, and both trials used for training and validation were initiated prior to routine HER2 testing. Therefore, this model needs additional validation in a HER2 negative patient subset.



To Hear Content from the Audio Clip Section of the Presentation **GS6-01** CLICK HERE

[GS6-03] Circulating tumor cells (CTCs) five years after diagnosis are prognostic for late recurrence in operable stage II-III breast cancer.

Late recurrences in breast cancer, as defined as a recurrence after 5 years from diagnosis, are common and account for about half of recurrences in estrogen receptor positive breast cancer. This risk is related to the number of involved lymph nodes with a risk as low as 5% with negative lymph nodes and 22% with 4 of more positive nodes based on data from a EBCTCG meta-analysis. In addition to stage, some gene expression assays are prognostics for late recurrence with increases of up to 2.5 fold in risk of recurrence in high risk groups compared to low risk groups. Circulating tumor cells (CTCs) are of interest as a potential predictor of late recurrence. Blood tests for enumerating CTCs are being utilized in research in the metastatic setting and CTC burden is related to prognosis in metastatic breast cancer. In previous studies, patients with CTCs after surgery and prior to initiation of systemic therapies have an increased risk of recurrence compared to those patients without CTCs. Based on this clinical background, the ECOG-ACRIN group conducted a study to evaluate if the presence of CTCs is prognostic for late recurrence in patients with early breast cancer.

The two main study objectives were to determine the prevalence of CTCs 5 years after diagnosis and to determine the association between CTCs and risk of recurrence. Patients with stage II-III HER2 negative breast cancer were prospectively selected from the E5103 (NCT00433511) clinical trial. These patients received adjuvant treatment with adriamycin and cyclophosphamide followed by paclitaxel +/-bevacizumab followed by at least five years of endocrine therapy if hormone receptor positive. Selected patients were recurrence free 4.5-7.5 years after diagnosis and whole blood was used for CTC identification and enumeration using the CellSearch method at the time of entry onto this substudy. The assay results were not reported to the patient or investigators. The sample size was set to detect a difference in CTCs rates from <1% to 5-10%. The primary endpoint of the trial was time to recurrence (TTR) as defined as time between the date of sample to first invasive distant and/or local recurrence.

After a median follow up of 1.8 years, 4.0% of patients with hormone receptor positive breast cancer had relapsed compared to only 0.5% of patients with triple negative breast cancer. There was no significant difference in the patient or tumor characteristics in the CTC-positive cohort compared to the CTCs negative cohort. In the hormone receptor positive group, CTC positive patients had a 21.7 fold higher risk of recurrence compared to CTC negative patients. (slide here 10) In a multivariate Cox model adjusted for relevant clinical co-variants, the increased risk of recurrences remained significant at 18.1 fold higher for patients with CTCs. The burden of CTCs appeared to trend with increased risk of recurrence with 66% of patients recurring with 2 or more CTCs compared to 16% with 1 CTC. The authors concluded the CTCs were detectable 5 years after diagnosis in about 5% of patients with hormone receptor positive, HER2 negative breast cancer and in about 4% of triple negative patients. They also argued that this prospective study provides level 1 evidence supporting the clinical validity of a positive CTC assay with recurrence risk in hormone receptor positive breast cancer. This provides a potential method for risk stratification and additional studies are warranted.

To Hear Content from the Audio Clip Section of the Presentation **GS6-03** CLICK HERE

[GS6-04] The EndoPredict score predicts residual cancer burden after neoadjuvant chemotherapy and after neoendocrine therapy in HR+/HER2- breast cancer patients from ABCSG 34

Dr. Dubsky presented the work of the ABCSG in evaluating EndoPredict score as a prediction of tumor response to neoadjuvant therapy. The rate of pathologic complete response (pCR) to neoadjuvant therapies is low for tumors that are estrogen receptor positive and HER2 negative. Average pCR with chemotherapy is about 20% and average pCR with endocrine therapy about 2%. The ability to predict a pCR would be beneficial in the selection of patients for neoadjuvant therapy when attempting breast conservation. Pathologic response for this study is based on the Residual Cancer Burden Score (RCB) which has been previously published and is defined as RCB0 (no residual cancer), RCB1 (minimal residual disease), and RCB2 and 3 (moderate and extensive residual disease).

ABCSG 34 was a phase II randomized trial of 400 patients with HER2 negative early breast cancer who received either neoadjuvant endocrine therapy or neoadjuvant chemotherapy as part of their standard of care therapy. The trial compared neoadjuvant tecemotide to neoadjuvant standard of care alone. One of the exploratory objectives of this trial was evaluation of the predictive value of Endopredict for pathologic response to neoadjuvant therapy. Endopredict is comprised of eight genes, three related to proliferation and five related to ER-signaling and differentiation. Included in this analysis were all women on the ABCSG 34 trial who were hormone receptor positive with complete clinical data including RCB assessment. RCB0 and 1 were considered "good response" and RCB2 and 3 were considered "poor response". The primary objective of the analysis was to test the predictive value of Endopredict concerning tumor response.

Evaluable patients included 134 in the neoadjuvant chemotherapy group and 83 patients in the neoendocrine group. The majority of the patients in the neoadjuvant chemotherapy had high risk Endopredict scores, 93.2%, whereas the neoadjuvant endocrine therapy group was more balanced with 44% having low Endopredict scores and 39% having high Endopredict scores. In the neoadjuvant chemotherapy group, none of the patients with a low Endopredict score achieved a good tumor response. Of the 92 patients with a high Endopredict score, 33 had a good tumor response giving a positive predictive value of only 26.4%. Switching to patients who received neoadjuvant endocrine therapy, patients with a high Endopredict score had a very low chance of a good tumor response. However, if the Endopredict score was low, there was a higher likelihood of tumor response.

The authors concluded that for women treated with neoadjuvant chemotherapy on the ABCSG trial, a low Endopredict score was highly associated with a poor tumor response and tumor shrinkage was driven by markers of cell proliferation such as ki-67. For patients in the neoadjuvant endocrine arm, high Endopredict score was associated with decreased tumor response and in this group tumor size was an independent predictor of tumor response. Thus, Endopredict score may provide additional information in the selection of patients for neoadjuvant chemotherapy versus neoadjuvant hormonal therapies.

To Hear Content from the Audio Clip Section of the Presentation **GS6-04** CLICK HERE

[GS1-04] Copy number aberration analysis to predict response to neoadjuvant anti-HER2 therapy: results from the NeoALTTO phase III trial

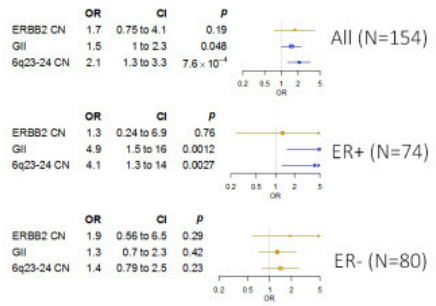
NEOALLTO was a prospective phase three randomized neoadjuvant clinical trial which evaluated pathological complete response rates in three different treatment arms: lapatinib + paclitaxel, trastuzumab + paclitaxel, and lapatinib + trastuzumab + paclitaxel. All patient then had surgery, followed by three cycles of FEC chemotherapy followed by the same HER2 directed therapy that they received in the neoadjuvant setting to complete a total of 52 weeks of HER2 directed therapy. The combination group with both lapatininb and trastuzumab had increased pathologic complete responses compared to patients that received either single agent trastuzumab or lapatinib. Patients with estrogen receptor negative breast cancer had an increase rate of pathologic complete response compared to patients with estrogen receptor positive disease. There was no significant different in the event free survival between the three groups.

In previously published work, a translational sub study analysis of NEOALLTO using RNA sequencing data demonstrated that the low expression of estrogen receptor, and increased expression of ERBB2 along with several immune signatures were significantly associated with a pathologic complete response. The objective for this study was to investigate copy number aberrations (CNAs) and their association with pathologic complete response (pCR) and event-free survival. Copy number aberrations were assessed using Cytoscan HD Affymetriz arrays with 2.75M probes and 750,000 SNPs. Of the 455 patients enrolled in NeoALLTo, there were 184 evaluable samples for this study.

The investigators utilized three different approaches to identify CNAs and assess association to rates of pCR. First, they looked for CNAs in a selection of 25 cancer genes that are known to be amplified in breast cancer. Additionally, they completed the genome instability index (GII) and recurrent CNAs were identified by GISTIC2. Among the selected cancer genes, only ERBB2 was predictive of a pCR. However, ERBB2 copy number did not significantly correlate with pCR once corrected for ERBB2 mRNA expression. A higher genome instability index was associated with an increased rate of pCR, and a higher genome instability index was found in estrogen receptor negative tumors when compared to estrogen receptor positive tumors. In the final approach using GISTIC, 159 recurrent regions were found to be either amplified or deleted. Some of these regions included know cancer related genes such as ERBB2, PTEN and RB1, but only one region was associated with a pCR. This region was identified as 6q23-24 which includes 39 genes.

A multivariate analysis that corrected for clinicopathological parameters showed a significant correlation in HER2 expression, HER2 enriched subtype by PAM50, HER2 copy number and copy number of 6q23-14 in pCR rate among estrogen receptor positive tumors. In estrogen receptor negative tumors, only an increase in HER2 expression was associated with a pCR. The authors concluded that a high copy number of ERBB2 was shown to be predictive of a pCR, but ERBB2 mRNA and HER2-enrichment as measured by PAM 50 were better predictors of pCR and high genome instability was associated with increased rates of pCR in estrogen receptor positive tumors. A novel amplified region on 6q23-24 was associated with pCR in estrogen receptor positive tumors and warrants additional investigation. No CNAs were associated with event free survival.

Multivariate analysis correcting for CP parameters and the expression of *ESR1*, *ERBB2* and *HER2-enriched*



CP = Age, tumor size, nodal status, ER status, histological grade and treatment arm

To Hear Content from the Audio Clip Section of the Presentation **GS1-04** CLICK HERE

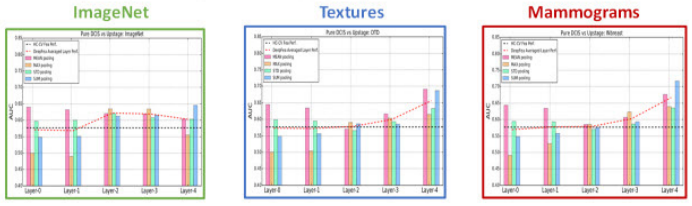
Imaging

[GS5-04] Prediction of occult invasive disease in ductal carcinoma in situ using deep learning features.

Among newly diagnosed ductal carcinoma in situ (DCIS) on diagnostic biopsy, about 26% will be "up staged" to invasive cancer on the surgical specimen. This up staging results in the potential change in management in regards to systemic therapy and repeat surgical procedures for lymph node evaluation. The prediction of up staging using clinical, imaging and histologic features have be shown as insufficient for clinical use. This presentation discussed the use of deep learning as a means to predict occult invasive disease. Deep learning is a novel method based on artificial neural networks (ANN) but with the addition of more layers which is now feasible with advances in algorithms and computing abilities.

This study included women at least 40 years old who underwent a stereotactic biopsy showing only DCIS for which digital magnification views were available at the home institution. Patients were excluded from the study if there was the presence of a mass, asymmetry or distortion, history of prior cancer or breast surgery, or the presence of any invasion on the biopsy. A total of 140 cases were included: 105 with pure DCIS and 35 with upstaging. The investigators then used a concept of "transfer learning" that allows them to apply the knowledge in already existing deep learning models to this relatively small data set. They started with a pre-trained deep learning model, VGG-16, that was trained on completely unrelated natural image identification, and fed in the study mammographic images. They pre-trained the VGG model with three unrelated data sets. These sets started out as very large and unrelated and then narrowed with few numbers but more task specific. The authors suggested that transfer learning using pre-trained deep learning models outperforms previous work with handcrafted computer vision features. As the pre-training scenarios become closer to the clinical task, the deep learning capabilities also become more useful. This early work can be expanded with larger data sets for development of specific deep learning models for breast imaging.

- Performances vary across 5 layers
  - each bar represents separate model (combination of dataset/layer/pooling)
  - average deep feature performance (----) >= previous handcrafted features (----)



To Hear Content from the Audio Clip Section of the Presentation **GS5-04** CLICK HERE

[PD2-13] Benefits of breast screening beyond mortality reduction

This study looked at the benefits of breast cancer screening in women receiving regular screening compared to those diagnosed with breast cancer outside of a regular screening group. Women included on the study were those treated for early stage breast cancer from a screening population (569 patients) compared to women diagnosed with breast cancer outside of this screening population at a single institution. The investigators found that women in the screening group had smaller invasive cancers, lower grades, more likely to be ER positive and less likely to have lymph node involvement. Patients diagnosed outside of a screening program where twice as likely to have a mastectomy, more likely to require an axillary dissection, more likely to receive neoadjuvant chemotherapy, and more likely to have post mastectomy radiation. The authors suggest that the increased treatment intensity and potential morbidity in the non-screened population should be considered in the debate regarding mammogram screening harm versus benefit.

[PD2-15] Effect of mammography screening frequency on false-positive biopsy rates and detection of local recurrence among breast cancer survivors.

There are currently no clear guidelines for screening in the post lumpectomy setting. This study sought to investigate how the frequency of screening mammograms affects rate of false-positive biopsy results and local recurrence among breast cancer survivors. This was a retrospective cohort study of women diagnosed with stage 0-III breast cancer between 2007 and 2015 who were treated with lumpectomy and had at least 2 screening mammograms at the local institution within the first three years from diagnosis. They then compared outcomes in women who received every 6 month mammograms versus women who had annual mammograms. They found no difference in the local recurrence rates with 4.1% in the 6 month screening group and 3.9% in the annual group. However, women with mammograms every 6 months had a greater than 2-fold increase in the risk of having a false positive biopsy (OR: 2.4). Factors associated with a higher false positive rate included younger age at diagnosis, higher tumor grade and those patients who received adjuvant chemotherapy. This data did not support a benefit with increased mammogram frequency post lumpectomy and found a higher rate of false positive biopsies with no difference in local recurrence rates in women who were screened every 6 months compared to those screened annually. (no audio clip or slide)

Local Therapies/Surgical Topics

[GS5-01] Appropriate margins for breast conserving surgery in patients with early stage breast cancer: A meta-analysis.

Dr. Vicini presented an updated meta-analysis evaluating margins for breast conserving surgery in patients with early stage breast cancer. This is an important and ongoing clinical question with the goal to balance the potential benefit of increased local control with the morbidity associated with re-excision. The last meta-analysis in 2014 concluded that wider margins were unlikely to provide substantial benefit in local breast cancer control, and this lead to the current SSO-ASTRO guideline of no tumor on ink. Additional patients and additional modeling have been complied since 2014 to evaluate if the no tumor on ink should remain the standard for surgical margins in breast conservation surgery.

The meta-analysis included studies from 1995-2016 with a minimum of 50 months of follow up, explicit pathologic definition of the margin status and local recurrence rate reported in relation to the margin status. Thirty-eight studies with 55,302 patients were identified that met these criteria. Compared to the 2014 meta-analysis, two studies and more than 20,000 patients were added to the analysis. The overall median follow up was 7.2 years. The margin definitions were similar to the previous analysis with a "positive" margin defined as invasive cancer or DCIS on the surgical margin, "negative" defined as no tumor within a specified distance from the margin, and "close" defined as no tumor on ink but tumor less than the specified distance from the margin. Three different models were utilized in this analysis. The first model included all patients with margins at or equal to the set margin distance compared to patients with a wider margin than required. The second model, which was unique to this analysis, was performed to assess the impact of the margin width "range" rather than a set margin width cut off point. This included four groups of margins: less than 0 mm, 0-2 mm, 2-5 mm, and >5 mm. Finally, the third model categorized margins into three groups: negative, close, and positive. The first model showed that negative margins were associated with lower rates of local recurrence, but the rate of local recurrence was similar regardless of the cutoff point that defined the margin as negative. Model 2 suggested that margin width was significantly associated with local recurrence when using set margin ranges. Model 3, also showed similar results to model 2 with margin status being associated with local recurrence. The authors of this meta-analysis suggest that a wider margin than no tumor on ink may decrease the rate of local recurrence. This recommendation would be in line with the current margin guidelines for ductal carcinoma in situ. They also argue that further prospective studies are required to validate appropriate margin width.

Crude Local Recurrence- Model 1

Negative vs close/positive

Margin (mm) and status	Number of studies providing data	Total number of observations	Total number of LR	LR %
≤0	28	3416	352	10.3
>0	38	46178	1758	3.8
≤1	29	3988	405	10.2
>1	27	33565	1161	3.5
≤2	32	5978	519	8.7
>2	23	31757	1053	3.3
≤5	38	9781	659	6.7
>5	8	19059	604	3.2

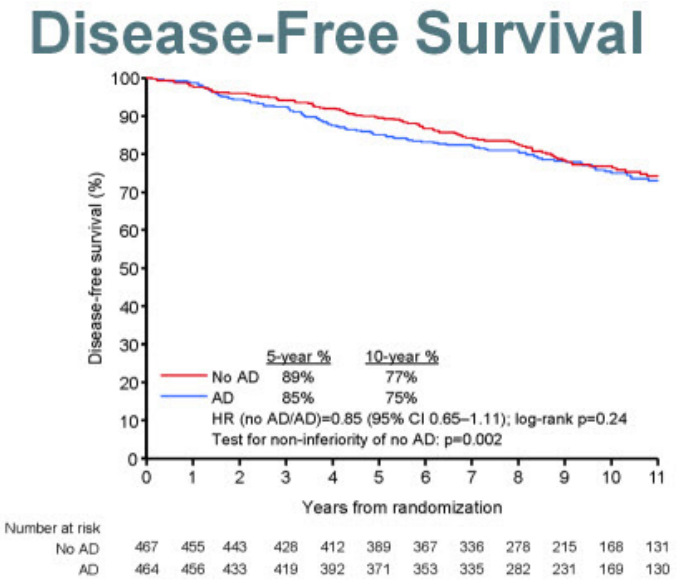
Benefit to wider margins observed with greatest difference (benefit) seen at 1 mm (6.7%), but similar rates of recurrence with all negative margin definitions (3.2-3.8%)

To Hear Content from the Audio Clip Section of the Presentation **GS5-01** CLICK HERE

[GS5-02] Axillary dissection vs. no axillary dissection in patients with cT1-T2cN0M0 breast cancer and only micrometastases in the sentinel node(s): Ten-year results of the IBCSG 23-01 trial

Dr. Galimberti presented the ten year results of the IBCSG 23-01 trial of axillary dissection versus no dissection in patients with cT1-T2 N0 breast cancer with only micrometastases in a sentinel node. Axillary dissection was previously the standard of care for a positive sentinel lymph node, but this changing with the long term results of studies like IBCSG 23-01 and ACOSOG Z0011 showing that the axillary dissection (AD) in patients with moderate axillary involvement provided no advantage in terms of overall or disease-free survival. Patients included in these study had a tumor size 5 cm or less with one or more micrometastatic (2 mm or less) sentinel nodes. They were then randomized to an axillary lymph node dissection versus no dissection. The primary endpoint was invasive disease-free survival (DFS) and the secondary endpoints were overall survival (OS) and recurrence in the un-dissected axilla. Sample size included 934 patients who were randomized in a 1:1 fashion. Patient and tumor characteristics in the two groups were well matched for factors which could contribute to recurrence. Patient who received breast conservation surgery where treated with standard breast radiotherapy. Subsequent adjuvant therapies were also well balanced between the two groups.

The criteria of non-inferiority between the AD group and no AD group was meet with a 10 year DFS of 77% in the no AD arm compared to 75% in the AD arm (HR 0.85 p=0.002). The cumulative incidence of breast cancer events was also similar between the two groups with 10 year incidence of 17.6% in the no AD arm and 17.3% in the AD arm. Ipsilateral axillary recurrence was very low in both groups: 0.4% in the AD arm and 1.7% in the no AD arm. The overall survival at 10 years was 91% in the no AD arm and 88% in the AD arm which was not a statically significant difference (P=0.20 and HR 0.77). The subgroup analysis was consistent with the primary analysis with no subgroup benefiting more from AD compared to no AD. The authors concluded that, with a median follow up of 9.8 years, there was no significant difference between AD and no AD for women with micrometastatic lymph node involvement in regards to DFS and OS. Also, the rate of axillary recurrence in the no AD arm was low at 1.7% overall and 0.8% in patients with breast conserving surgery. These findings are consistent with the results of ACOSOG Z0011 and supports the current standard of no AD in early breast cancer when the sentinel node is only minimally involved.



To Hear Content from the Audio Clip Section of the Presentation **GS5-02** CLICK HERE

Topics is Systemic Therapies

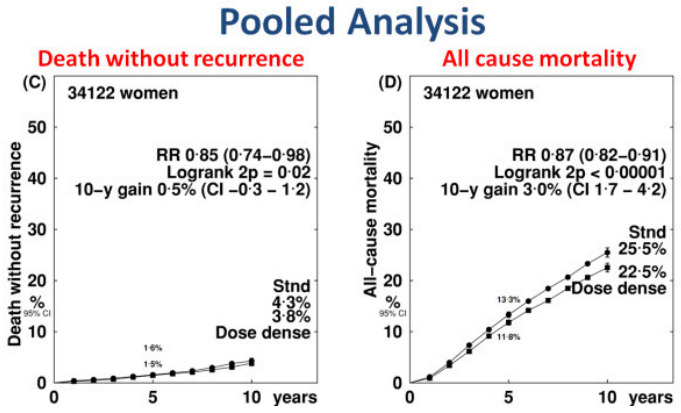
[GS1-01] Increasing the dose density of adjuvant chemotherapy by shortening intervals between courses or by sequential drug administration significantly reduces both disease recurrence and breast cancer mortality: an EBCTCG meta-analysis of 21,000 women in 16 randomised trials

The first abstract presented at the podium this year reviewed the results of the EBCTCG meta-analysis of increasing the dose intensity of adjuvant chemotherapy, and its effect on breast cancer disease free survival and overall survival. It has been established that adjuvant chemotherapy with an anthracycline and taxane-based regimen significantly decreases the risk of breast cancer related mortality. There is also cytokinetic models which suggest that increasing the dose intensity of chemotherapy can enhance efficacy, but this has always required balance with the maximum tolerated dose in the clinical setting. This large meta-analysis gives valuable insights into the balance of the risk and benefit of dose intensity.

The authors highlighted three means to increase dose intensity in chemotherapy administration. First, the dose in each cycle can be increased. Second, the intervals between treatments can be decreased and third, the drugs can be given in a sequential manner rather than concurrently. Higher doses of anthracyclines (75mg/m2 and 90 mg/m2) were evaluated in the INT0418 clinical trial which showed no significant change in disease free survival when higher doses were administered. Thus, this study focused on the effect of shorter intervals ("dose dense" chemotherapy) and sequential rather than concurrent administration schedules.

The analysis included 34,122 individual patient data from 25 trials with the primary outcomes including breast cancer recurrence and breast cancer mortality as analyzed by standard logrank methods. Pooled analysis of all 25 dose-dense and sequential trials showed a ten year recurrence rate of 32% in the standard arm compared to 28.4% in the dose dense arm which was statistically significant with a p-value of less than 0.01. Breast cancer mortality was also decreased in the dose dense group with a mortality rate of 19.2% at 10 years v. 22.2% which was also statistically significant. The investigators also looked at all-cause mortality to evaluate for deaths potentially related to the risks associated with dose dense chemotherapy and found that all-cause mortality was slightly higher, 25.5%, in the standard arm compared to 22.5% in the dose dense arm. The benefit of dose density was preserved when recurrence by estrogen receptor status was evaluated. Both estrogen receptor positive and estrogen receptor negative patients benefited from dose density of chemotherapy administration.

Thus the authors concluded that shortening the interval between cycles and the sequential administration of anthracycline and taxane chemotherapy reduced both breast cancer recurrence and death from breast cancer. Increasing dose density was beneficial in both estrogen receptor positive and estrogen receptor negative breast cancers, and there was no significant increase in overall mortality in patients that received dose dense chemotherapy.



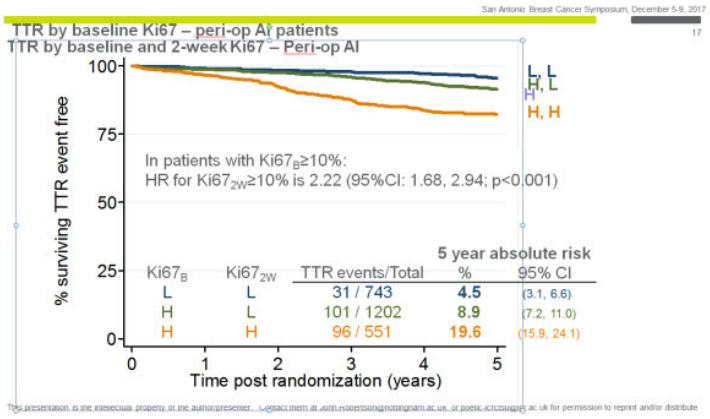
To Hear Content from the Audio Clip Section of the Presentation **GS1-01** CLICK HERE

[GS1-03] Perioperative aromatase inhibitor treatment in determining or predicting long term outcome in early breast cancer – the POETIC trial.

Dr. Roberston presented the results of the POETIC trial which was a phase three randomized clinical trial designed to address two clinically meaningful questions. Previous trials suggested that peri-operative endocrine therapy may improve patient outcomes, and the IMPACT Trial suggested that the tumor Ki67 after two weeks of endocrine therapy may be a better predictor of outcome than the baseline Ki67. Therefore, POETIC sought to address if perioperative endocrine therapy improved clinical outcomes in ER positive breast cancers, and if the change in Ki67 after two weeks of endocrine therapy can better predict relapse risk when compared to baseline ki67 alone. Postmenopausal women with newly diagnosed invasive breast cancer were randomize 2:1 to perioperative therapy with an aromatase inhibitor (AI) for 2 weeks before and after surgery vs. no peri-operative AI treatment. Further treatment was determined by the treating physician. Baseline biopsies were collected from diagnosis and after two weeks of AI therapy. The primary endpoint was time to recurrence (TTR) as defined as time from randomization to any breast cancer recurrence. Secondary endpoints included Ki67 at baseline and Ki67 after two weeks of an AI as a predictor of outcome. The study enrolled 4,480 patients: 2,976 women to the peri-operative AI arm and 1,504 to the no peri-operative AI arm. For the analysis, 2,528 paired Ki67 samples were available for the peri-operative AI group, and 678 paired samples were collected for the no AI group based on a 2 week random selection of patients for control samples. Results were reported with a median follow up of 60 months.

The time to recurrence between the two groups was the same with the TTR event free percentage in the peri-operative AI group being 90.9% vs. 90.3% in the no peri-operative AI group (p=0.37 and HR 0.91). The overall survival at five years was also similar between the two groups with 89.0% surviving in the treatment group vs. 89.5% in the no AI group.

Patients with a low baseline Ki67 that remained low after two weeks of an AI proved to have the best clinical outcomes. This was followed by patients with high Ki67 that subsequently converted to low Ki67 after two weeks of AI therapy. Patients who had a high Ki67 and remain high after two weeks of AI therapy had a shorter time to relapse as shown on the Kaplan Meier curve.



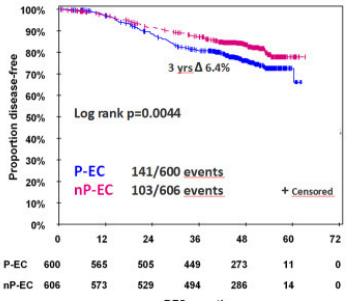
The study authors concluded that there was no significant improvement in clinical outcomes with peri-operative AI therapy and the change in Ki67 after two weeks of AI treatment can provide independent prognostic information in regards to time to recurrence. In the group of patients with a high baseline Ki67, two weeks of peri-operative AI treatment with repeat measurement of the Ki67 could potentially identify patients with a higher risk of recurrence (if Ki67 stays high) versus a lower risk of recurrence (if Ki67 decreases). The authors suggest that patients with persistently high Ki67 could be selected for additional adjuvant therapies.

[GS3-05] Survival analysis of the prospectively randomized phase III GeparSepto trial comparing neoadjuvant chemotherapy with weekly nab-paclitaxel with solvent-based paclitaxel followed by anthracycline-cyclosphosphamide for patients with early breast cancer - GBG69

The first survival data was presented for the GeparSepto clinical trial which compared two different forms of paclitaxel in patients receiving neoadjuvant chemotherapy for high risk early breast cancer. This was a large phase three randomized trial with patients randomized equally to two arms. In the first arm, patients received standard solvent-based paclitaxel at a dose of 80mg/m2 weeks for twelve weeks followed by four cycles of epirubicin and cyclophosphamide. For patients with HER2 positive breast cancer, trastuzumab and pertuzumab was administered every three weeks during the duration of the neoadjuvant chemotherapy. The second group received the same treatment regimen but with nab-paclitaxel at a dose of 150mg/m2 weekly instead of standard weekly paclitaxel. There was a subsequent dose reduction of the nab-paclitaxel to 125mg/m2 after the recruitment of 464 patients in an effort to decrease the rate of neuropathy. Patients were stratified based on hormone receptor status, HER2 status, low vs. high Ki67 score and SPARC expression.

The primary endpoint was pathologic complete response rate (pCR) and secondary efficacy endpoints were disease free survival, distant disease free survival and overall survival. The pCR data was been previously presented at SABCS and has been published. The substitution of solvent-based paclitaxel with nab-paclitaxel significantly increased the pCR rate from 29% to 38%. The largest absolute improvement was seen in patients with triple negative breast cancer with 26% pCR in the solvent-based paclitaxel arm vs. 48% in the nab-paclitaxel arm (p<0.001).

At a median follow up of 49 months, there was a significant improvement in the three year disease free survival of 6.4% in the nab-paclitaxel arm (87.1% DFS) compared to the solvent-based paclitaxel (80.7% DFS) with a p=0.0044. The reported number needed to treat was 16 patients to prevent one disease relapse. Although the numbers are low and the difference not statistically significant, triple negative breast cancer patients may benefit more from nab-paclitaxel compared to solvent-based paclitaxel (DFS 78.7% vs. 68.6% p=0.0694). A pre-specified subgroup analysis favored nab-paclitaxel in all groups. The overall survival data has not yet matured. The surrogate value of pCR is confirmed in this study with patients who achieved a pCR, regardless of the type of paclitaxel, having an improved DFS and OS compared to patients who did not achieve a pCR. The authors concluded that nab-paclitaxel demonstrated a significantly improved DFS compared to standard solvent-based paclitaxel in all breast cancer subtypes.



- Median follow-up of 49 months (IQR 44.6 - 52.9)
- HR (nP-EC vs. P-EC) = 0.69 (95% CI 0.54-0.89)
- Number needed to treat (NNT; 3yrs) = 16 pts

DFS rates (estimated):

Time	P-EC	95% CI, P-EC	nP-EC	95% CI, nP-EC
3 yrs	80.7%	(77.2-83.7)	87.1%	(84.1-89.6)
4 yrs	76.2%	(72.3-79.5)	83.5%	(80.2-86.4)

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[GS3-06] Long-term follow-up of CALGB 40502/ NCCTG N063H (Alliance): A randomized phase III trial of weekly paclitaxel (P) compared to weekly nanoparticle albumin bound nab-Paclitaxel (NP) or ixabepilone (IX) +/- bevacizumab as first-line therapy for locally recurrent or metastatic breast cancer (MBC)

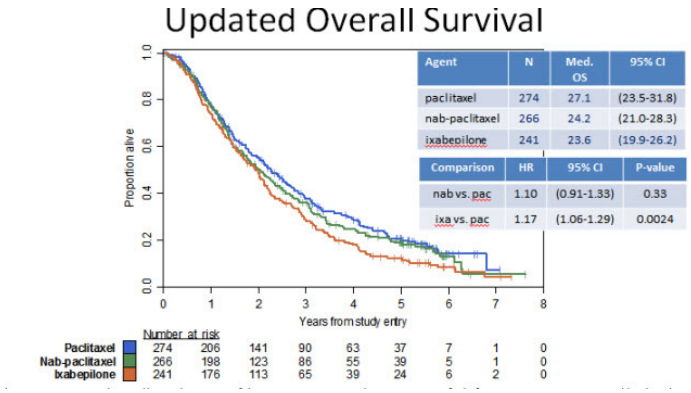
Dr. Rugo presented the long-term follow up for the CALBG 40502/NCCTG N0634 (Alliance) trial which evaluated three different chemotherapy agents with or without the addition of bevacizumab in patients with advanced breast cancer. This trial was designed based on previous clinical trials suggesting that nab-paclitaxel had promising efficacy in the first line setting, ixabepilone may be able to overcome

resistance to taxanes, and bevacizumab prolonged PFS when add to paclitaxel. At the time of this trial design, bevacizumab was approved for use in the United States and was standard therapy in the first line setting.

This study had three arms to which 799 patients were randomized in a 1:1:1 fashion. The control arm was weekly paclitaxel + bevacizumab and this arm was compared to two experimental arms: nab-paclitaxel + bevacizumab and ixabepilone + bevacizumab. Eligible patients had no previous lines of chemotherapy for advanced disease and were at least 12 months from receiving a taxane in the adjuvant setting. A major amendment to the trial was implemented in March 2011 allowing for the withdrawal of approval by the FDA for bevacizumab for metastatic breast cancer. However, 98% of patients received bevacizumab. The first interim analysis in July 2011 recommended the closure of the ixabepilone arm for futility and the two taxane arms were subsequently closed for futility in November 2011 at the time of the second interim analysis. The primary objective was progression free survival (PFS) of the control arm compared to each of the experimental arms and was previously reported at SABCS in 2013 with no significant difference between the three arms.

This analysis presented updated PFS and overall survival data with four years of additional follow up. Dr. Rugo reported that there was no significant difference in PFS between the two taxane arms and ixabepilone was inferior to the two taxane groups (p=0.001). The overall survival was similar with no significant difference in the two taxane groups (p=0.33) and ixabepilone was inferior to the two taxane arms (p=0.0024). In a subset analysis conducted to look at the effects in different subsets of breast cancer, nab-paclitaxel appeared to perform better than paclitaxel in triple negative breast cancer although the study was not powered to detect this difference. In regards to adverse events, patients receiving nab-paclitaxel experienced more sensory neuropathy, motor neuropathy and hematologic events compared to paclitaxel or ixabepilone, and more patients discontinued treatment secondary to adverse events in the nab-paclitaxel arm.

This updated analysis supports the early trial findings. First, ixabepilone appears to be inferior to paclitaxel in both PFS and OS. Adverse events and treatment discontinuation was high with nab-paclitaxel doses of 150mg/m2 and this dose should no longer be used in patients with breast cancer and a dose of 125mg/m2 should be considered instead. Further investigation may be warranted to explore efficacy in different breast cancer subtypes.



[GS4-06] Cancer risks and response to targeted therapy associated with BRCA2 variants of uncertain significance

As the utilization of genetic testing increases, the clinical questions regarding implications of variants of uncertain significance (VUS) is also increasing. Most VUS are identified through germline mutation testing completed through panel testing, which is becoming increasing common, while others have been identified via tumor sequencing. They commonly arise as a missense mutation, intronic and in-frame deletions or insertions. More than 3,000 individual VUS have been identified in BRCA 1 and 2 genes, and the vast majority will not ultimately be determined to be pathogenic. Thus, VUS present a significant clinical challenge in regards to clinical management questions such as risk assessment, changes in screening methods and prophylactic treatments. Also, identification of a VUS can cause increased anxiety for the patient. Currently, the identification of a VUS should not be used to guide clinical care.

Dr. Couch reviewed in this presentation novel methods for evaluating VUS in the BRCA2 gene. The first involves a new HDR functional assay to classify BRCA2 missense variants in the DNA binding domain which is thought to be an important region of the BRCA2 gene for pathologic mutations. They used 19 established non-pathogenic and 13 pathogenic missense variants in the DNA binding domain to develop a probability based model. In reference to the graph below, any VUS below the horizontal black line has a 99% probability of being pathogenic. Similarly, above the horizontal black lines represents 99% probability of neutrality. (Insert slide 10 here)

They then applied this model to 139 VUS in the BRCA2 DNA binding domain, and the HDR model identified a total of 54 variants predicted to be pathogenic. This is compared to the current ten variants that have been identified as pathogenic through the means of expert review of data. The large number identified in the neutral category (above the black line) is also useful information for patients harboring these VUS.

The group further evaluated the variants identified as deleterious with the HDR assay in a partnership with Ambry Genetics data and the use of public reference controls. A VUS determined to be deleterious with the HDR assay had an odds ratio of being associated with breast cancer of 5.32 compared to an odds ratio of 1.51 in a VUS that was categorized as neutral. This provides additional support that

the HDR assay is preforming well in the population that is receiving testing. In addition, the investigators were able to demonstrate resistance and sensitivity to cisplatin in BRCA2 missense variants that were identified as neutral versus deleterious. Suggesting that this HDR assay can also predict functional response to cisplatin. Similar studies with PARP inhibitors are ongoing.

With these assays put together, the authors feel they have improved the prediction of risk based on a functional assay and can potentially predict response to different therapeutics. This HDR assay provides the addition of quantitative methods to the quality data that is currently in use for identifying variances of uncertain significant in the BRCA genes.

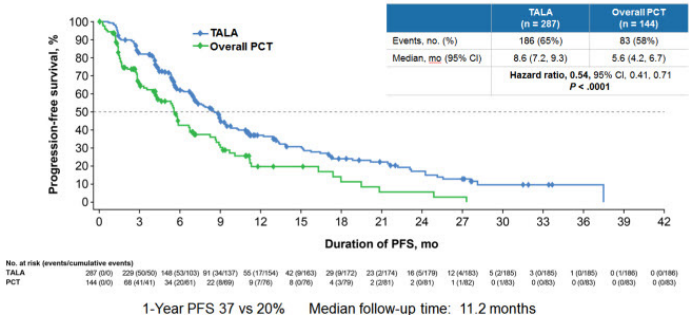
[GS6-07] EMBRACA: A phase 3 trial comparing talazoparib, an oral PARP inhibitor, to physician's choice of therapy in patients with advanced germline BRCA-mutation breast cancer

Talazoparib is a highly potent dual mechanism PARP inhibitor which inhibits the PARP enzyme and traps PARP on single-stranded DNA breaks leading to prevention of DNA damage repair and subsequent cell death. In a phase one trial of multiple tumor types, a 1 mg/day continuous daily dosing schedule was established. The phase 2 ABRAZO trial showed promising efficacy and safety in breast cancer patients with germline BRCA 1/2 mutations with either multiple prior lines of chemotherapy or prior platinum therapy. Dr. Litton presented the results of the international phase III EMBRACA trial which enrolled 431 patients with locally advanced or metastatic HER2-negative breast cancer and a germline BRCA1 or BRCA2 mutation. Patients were stratified based on number of line of prior chemotherapy regimens, hormone receptor status and history of central nervous system metastases to either talazoparib or physician choice of therapy (PCT). Physician choice of therapy could include capecitabine, eribulin, gemcitabine, or vinorelbine. The primary endpoint was progression free survival (PFS), secondary endpoints were overall survival (OS), overall response rate (ORR) and safety. Exploratory endpoints included duration of response (DOR) and quality of life (QOL).

With a median follow up of 11.2 months, the PFS in the talazoparib group was 8.6 months compared to 5.6 months in the PCT group. This is statistically significant with a HR of 0.54 and a p<0.0001. The subgroup analysis all favored treatment with talazoparib. In the preplanned subgroup analysis of patients with previously treated CNS metastases, the PFS in the talazoparib group was significantly longer at 5.7 months versus 1.6 months in the PCT group (HR 0.32). The secondary endpoint of overall survival did not meet statistical significance, however, there was a late separation of the curve and OS will be re-evaluated with a longer duration of follow up. Of note, there were 12 (5.5%) complete responses in the talazoparib group compared to none in the PCT group. The objective response rate in the talazoparib arm was 62.6% compared to 27.2% in the PCT arm.

The primary adverse event for talazoparib is anemia. Two patients discontinued talazoparib secondary to anemia. Neutropenia was also a common adverse event with talazoparib, but the rate of febrile neutropenia was very low (0.3%). The common nonhematologic toxicities included fatigue, nausea, alopecia and headaches, the majority being grade 1 and 2. Patient reported global health status was recorded and showed an improvement in patients on the talazoparib versus a decrease in the global health status in patients treated in the PCT arm. The authors concluded that talazoparib met its primary endpoint with increase in PFS compared to PCT. Additionally, talazoparib was generally well tolerated and improved patient reported global health status. Overall survival data was immature at the time of this presentation.

Primary Endpoint: PFS by Blinded Central Review



1-Year PFS 37 vs 20% Median follow-up time: 11.2 months

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ER Positive

[GS2-05] First-line ribociclib vs placebo with goserelin and tamoxifen or a non-steroidal aromatase inhibitor in premenopausal women with hormone receptor-positive, HER2-negative advanced breast cancer: Results from the randomized phase III MONALEESA-7 trial

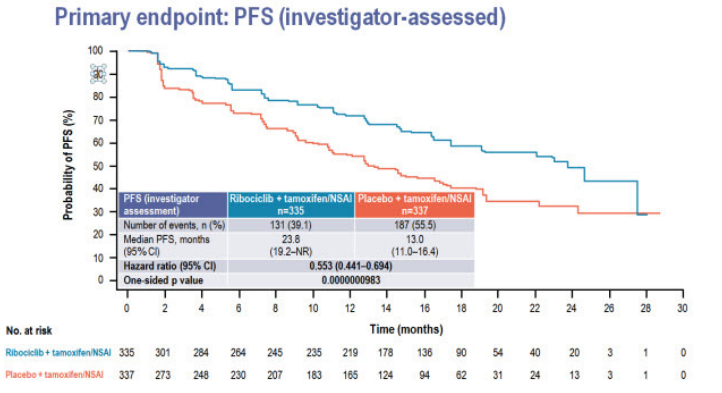
The initial results of the MONALEESA-7 clinical trial were presented by Dr. Debu Tripathy. The MONALEESA-7 trial is the first phase III trial investigating CDK4/6 inhibitor-based regimens as a front-line treatment specifically for premenopausal women with advanced estrogen receptor positive breast cancer. Young women, when compared to postmenopausal women, tend to have more aggressive tumors, harbor a different tumor biology, and are more likely to die from their breast cancer. Previous studies have shown an increase in progression free survival with the addition of ribociclib to letrozole in postmenopausal women with hormone receptor positive (HR+) breast cancer. Thus the MONALESSA-7 trial was initiated to evaluate ribociclib in premenopausal women.

The study enrolled 672 premenopausal women with HR+ and HER2 negative advanced breast cancer with one or less lines of chemotherapy and no prior endocrine therapy for advanced disease. All patients received tamoxifen or an aromatase inhibitor with ovarian suppression and were randomized 1:1 to receive the addition of ribociclib or placebo. The primary

endpoint was progression free survival (PFS) and secondary endpoints included overall survival, overall response rates, clinical benefit rate, safety and patient-reported outcomes.

The results were consistent with a significant improvement in progression free survival with 23.8 months in the ribociclib arm compared to 13.0 months in the placebo arm (HR 0.553) as assessed by the investigator. Progression free survival data gathered by a blinded independent review committee supports the investigator generated data. In a subgroup analysis, all groups favored treatment with ribociclib compared to placebo. The choice of endocrine therapy backbone, tamoxifen or an aromatase inhibitor, did not show a significant difference in PFS. Overall survival data was immature at the data cut-off and will be presented at a later date. Dose density was high in both groups, 94% in the ribociclib arm and 100% in the placebo arm. Patient-reported outcomes were assessed and favored the treatment arm with ribociclib. Cytopenias were more common in the ribociclib arm with 9.9% of patients having grade 4 neutropenia in the ribociclib group compared to 0.6% in the placebo group. However, febrile neutropenia was rare at 2.1% in the ribociclib group. More patients in the ribociclib arm had QT prolongation compared to the placebo group (6.9% vs. 1.2%). During this study, QT prolongation was not associated with clinical symptoms or arrhythmias.

This study demonstrated that ribociclib added to tamoxifen or an aromatase inhibitor with ovarian suppression as front line therapy in premenopausal women significantly prolongs progression free survival when compared to placebo. Both endocrine partners, tamoxifen or an AI, showed efficacy when paired with ribociclib, and all subgroups favored the arm with ribociclib. The authors therefore concluded that ribociclib in combination with tamoxifen or an AI with ovarian suppression should be considered as potential new treatment option for premenopausal women with hormone receptor positive, HER2 negative advanced breast cancer.



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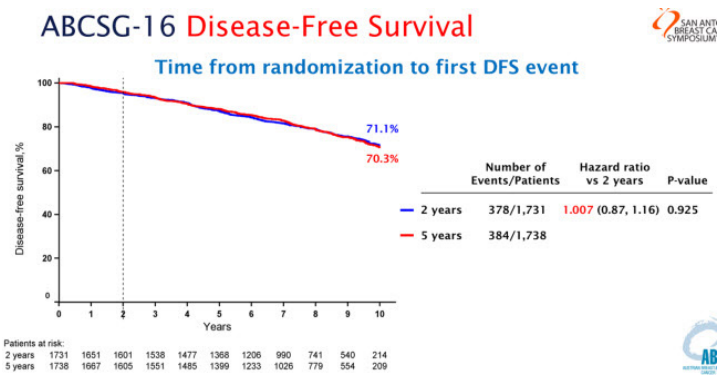
[GS3-01] A prospective randomized multi-center phase-III trial of additional 2 versus additional 5 years of Anastrozole after initial 5 years of adjuvant endocrine therapy - results from 3,484 postmenopausal women in the ABCSG-16 trial

The risk of relapse for hormone receptor positive breast cancer extends for many years after diagnosis and more than half of recurrences occur after the first five years of follow up. Thus many trials have sought to evaluate the benefit of extending endocrine therapy more than five years. The current body of scientific study has shown that aromatase inhibitors (AI) out perform tamoxifen in postmenopausal women and prolonging tamoxifen therapy in premenopausal women is of benefit. The addition of an AI after tamoxifen in postmenopausal women is also beneficial. What is less certain is the benefit of extended AI therapy after initial therapy with an AI in postmenopausal women. This leads to the question at hand as to the optimal duration of treatment with an AI.

The Austrian Breast and Colorectal Cancer Study Group (ABCSG) conducted the ABCSG-16 study to evaluate the benefit of an additional 2 vs. 5 years of anastrozole following 4-6 years of endocrine therapy. This was a large, randomized, multicenter trial that enrolled 3,484 postmenopausal women with hormone receptor positive breast cancer. All patients had previously received 4-6 years of tamoxifen, an AI, or a combination of tamoxifen and an AI in sequence. They were then randomized 1:1 to receive an addition of 2 vs 5 years of extended anastrozole therapy. The median follow up at the time of data reporting was 9 years, or an average of 14 years after their initial diagnosis. The primary endpoint of the trial was disease free survival (DFS) of the additional 2 years versus the addition of 5 years of anastrozole following 5 years of endocrine therapy. Secondary endpoints reported included overall survival, and time to contralateral breast cancers, secondary primary cancer and clinical fracture rate.

The results showed no significant difference in the DFS in the two groups with 71.1% DFS in the 2 year therapy group and 70.3% in the 5 year therapy group (HR 1.007 and P=0.925). No subgroup was identified to benefit from 5 years vs. 2 years of additional therapy and this subgroup analysis did include high risks patients such as node positive patients and patients who received prior chemotherapy. Similarly, there was no significant difference in overall survival between the two groups with 85.3% in the 2 year group and 84.9% in the 5 year group (HR 1.007 and P=.0947). There was no difference in the risk of contralateral breast cancer or second primary breast cancers. The trial explored treatment adherence and this analysis showed that about 20% of patients were no longer on therapy 2 years after randomization, and by 5 years non-adherence increased to about 40%. Because of this high non-adherence to therapy, a subset analysis was completed that included only “adherent” patients, but there was still no significant difference in DFS (70.6% in the 2 year group and 71.8% in the 5 year group). There was a difference the risk of clinical fractures with 4.7% in the 2 year arm vs. 6.3% in the 5 year arm which reached borderline significance level with a p-value of 0.053. The authors concluded that 5 years of additional AI therapy did not improved DFS or OS when compared to 2 years of additional AI therapy in postmenopausal women and, thus, there is no benefit to continuing endocrine therapy in this group beyond 7 years.



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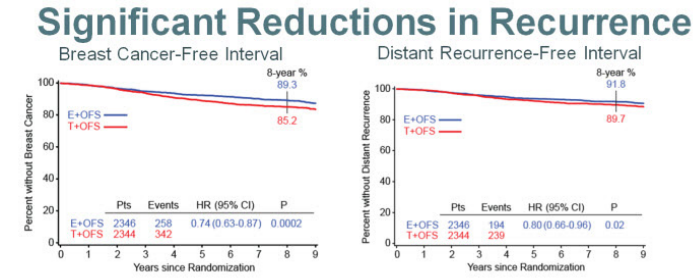
[GS4-02] Randomized comparison of adjuvant aromatase inhibitor exemestane (E) plus ovarian function suppression (OFS) vs tamoxifen (T) plus OFS in premenopausal women with hormone receptor positive (HR+) early breast cancer (BC): Update of the combined TEXT and SOFT trials

Dr. Francis presented the updated results of the combined TEXT and SOFT clinical trials which were randomized trials comparing exemestane to tamoxifen, both in combination with ovarian function suppression (OFS), in premenopausal women with early hormone positive breast cancer. Previously published data after a median follow up of 5.7 years found that adjuvant exemestane with OFS significantly improved disease free survival (DFS) when compared to tamoxifen with OFS. Many treatment guidelines have incorporated this treatment strategy for premenopausal women with early stage breast cancer. This presentation updated the results after median follow up of 9 years.

The TEXT trial enrolled 2,672 patients between 2003 and 2011. All patients were premenopausal hormone receptor positive and could have received chemotherapy or not. Hormonal therapy was started within 12 weeks of surgery. Patients were randomized to two arms: tamoxifen + OFS for five years vs. exemestane + OFS for five years. The primary endpoint was disease free survival (DFS) and secondary endpoints included breast cancer free interval, distant recurrent-free interval and overall survival. In this combined analysis, 27% of the patients were less than 40 years of age and about half received chemotherapy. The patients that received chemotherapy tended to have higher risk disease and were more likely to younger, have lymph node involvement and tumors greater than 2 cm when compared to the patients that did not receive chemotherapy.

After 9 years median follow up, exemestane combined with OFS had an 86.8% DFS vs. 82.8% DFS with tamoxifen plus OFS which is a 4.0% absolute improvement with a HR of 0.77. There was also a statistically significant difference in the breast cancer-free interval (89.3% vs. 85.2%) and distant recurrence-free survival interval (91.8% vs. 89.7%) in favor of the exemestane and OFS group. There is still no difference in overall survival between the exemestane + OFS and the tamoxifen + OFS groups. The subgroup receiving chemotherapy had a larger number of events which is expected given their higher risk clinical features, and this group showed a greater benefit compared to patients that did not received chemotherapy. Patient receiving prior chemotherapy had a 6.9% difference between the exemestane + OFS group compared to the tamoxifen + OFS group in the TEXT trial and a 9.2% difference in the SOFT trial. Also, there was a persistent treatment effect by age with younger patients having greater absolute benefits. The adverse events were as expected with increased rates of endometrial cancer and thrombotic events in the tamoxifen group and increased musculoskeletal symptoms, osteoporosis and fractures in the exemestane group. Overall, 15% of patients stopped all assigned therapy early. At the four year mark, 25% of patients in the exemestane group had stopped assigned therapy compared to 19% in the tamoxifen group. There was no different in the rate of triptorelin cessation rate (18-19%).

The authors concluded that this analysis, with a longer follow up of 9 years, confirms the statistically significant improvement in DFS with exemestane + OFS compared with tamoxifen + OFS with an absolute improvement in DFS of 4% and a reduction in distant recurrence of 2.1%. This improvement in the exemestane group was seen in all subgroups with patients who received prior chemotherapy having the most benefit with improvements in DFS of 7-9% and absolute improvements in distant recurrence free interval of 5-7%. All age groups benefited, but the benefit was greater in women less than 40 years of age.



4.1% absolute improvement in 8-yr freedom from breast cancer for E+OFS
2.1% absolute improvement in 8-yr freedom from distant recurrence for E+OFS

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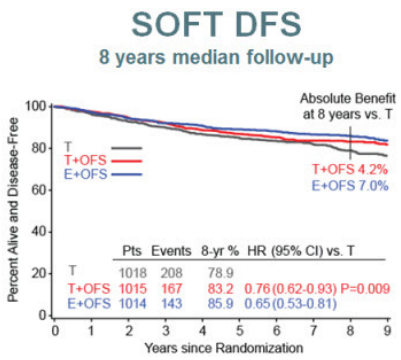
[GS4-03] Randomized comparison of adjuvant tamoxifen (T) plus ovarian function suppression (OFS) versus tamoxifen in premenopausal women with hormone receptor-positive (HR+) early breast cancer (BC): Update of the SOFT trial

Following the presentation of the combined TEXT and SOFT trials, Dr. Fleming presented the 8 year follow up results of Suppression of Ovarian Function Trial (SOFT). This trial enrolled 3,047 premenopausal women with completely resection hormone receptor positive breast cancer between

2003 and 2011. Hormone receptor positivity was defined as at least 10% progesterone or estrogen receptor positivity. Women were evenly stratified by prior chemotherapy, nodal status and method of ovarian function suppression (OFS) into three arms: tamoxifen for 5 years, tamoxifen + OFS for five years, and exemestane + OFS for 5 years. Due to a fewer number of disease free events observed than originally planned, the original statistical plan for a three way comparison among the groups was not feasible, and thus the primary analysis was the comparison between the two tamoxifen arms with a secondary analysis of the exemestane + OFS arm vs. tamoxifen alone. The comparison of exemestane + OFS vs. tamoxifen + OFS was addressed as a combined analysis of TEXT and SOFT and is summarized above. The primary study endpoint was disease free survival (DFS) and the secondary end points were breast cancer-free interval, distant recurrence-free interval and overall survival.

The initial primary results of this trial have been previously published in the NEJM in 2015 with no significant difference in DFS after 5.6 years of follow up between tamoxifen alone and tamoxifen + OFS. There was a significant difference in a subset of patients who received chemotherapy and remained premenopausal after chemotherapy. This presentation updated the previously published results with a longer median follow up of 8 years. With this longer follow up, the tamoxifen + OFS had a statically significant improvement in DFS of 83.2% compared to tamoxifen alone at 78.9 (HR 0.76 and P = 0.009). The absolute benefit was 4.2%. Exemestane + OFS compared to tamoxifen alone had a greater benefit of 85.9% vs. 78.9% DFS (HR 0.65). Looking at the cohorts that had and had not received prior chemotherapy, there was more absolute benefit in the group that received prior chemotherapy due to their increased risk for recurrence based on baseline tumor characteristics. The greatest benefit was seen in the cohort of patients less than 35 years of age who received chemotherapy. In this group, the absolute benefit in DFS was 13.1% in the exemestane + OFS compared to the tamoxifen alone arm (77.4% vs. 64.3% respectively). In regards to the secondary endpoints of distant recurrence-free survival (DRFS) and overall survival (OS), there was a small absolute benefit in the prior chemotherapy cohort. In this cohort, there was an absolute benefit of 4.5% in DRFS in the exemestane + OFS and 2.1% in the tamoxifen + OFS when compared to tamoxifen alone. For OS in this same group, there was a 4.3% benefit in the tamoxifen + OFS and 2.1% in the exemestane + OFS when compared to tamoxifen alone. Of note, the overall survival data remains immature and continued follow up is needed.

The authors concluded that the addition of ovarian function suppression to tamoxifen significantly improves disease free survival as seen with a longer median follow up of 8 years. Additionally, disease free survival is further improved by exemestane plus ovarian suppression. A small overall survival benefit is seem in the cohort of patients with significant risk disease to have received prior chemotherapy, and patients not receiving chemotherapy had a low risk of recurrence after 8 years with tamoxifen alone. Continued follow up is needed as overall survival data is not yet mature.



T+OFS significantly improves DFS vs T-alone in the overall population

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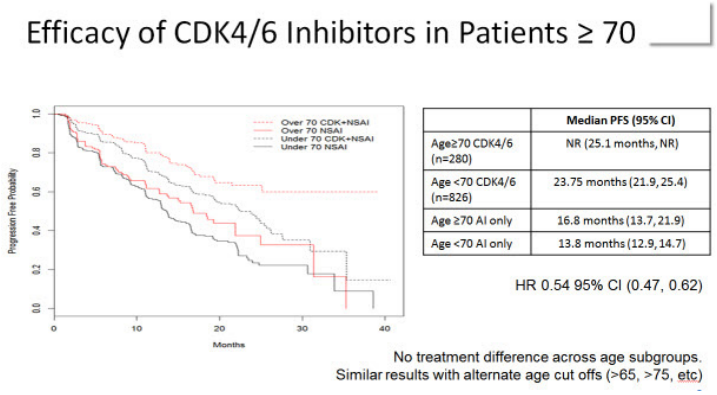
[GS5-06] A U.S. Food and Drug Administration pooled analysis of outcomes of older women with hormone-receptor positive metastatic breast cancer treated with a CDK4/6 inhibitor as initial endocrine based therapy

Dr. Singh presented a pooled analysis of FDA data on outcomes for older women treated with CDK 4/6 inhibitors as their initial treatment for metastatic hormone receptor positive breast cancer. The treatment of elderly women with breast cancer is important as the incidence of breast cancer increases with age and 40% of breast cancer related deaths occur in women who are at least 70 years of age. Often breast cancer in the elderly is hormone receptor positive and this subgroup of patients are likely to have CDK 4/6 inhibitors as a potential therapeutic option. Enrollment of the elderly onto clinical trials is often difficult and therefore elderly patients tend to be underrepresented in early clinical trials when the therapeutic doses are evaluated and adverse events are initially observed.

This pooled retrospective analysis included patients 70 years old or older enrolled on registration trials submitted to the FDA for CDK 4/6 inhibitors in combination with an aromatase inhibitor as initial therapy for hormone positive advanced or metastatic breast cancer. The intent to treat population was 1,992 women and the primary outcome measured was progression free survival in the treatment group compared to the control group. The primary outcome of progression free survival (PFS) in patients 70 years or older on treatment with a CDK 4/6 inhibitor and an AI was not reached (25.1 months). This is in comparison to a PFS of 16.8 months in women 70 and older on therapy with an AI alone, and in comparison to women less than 70 on a CDK 4/6 inhibitor and a AI with a PFS of 23.75 months.



In regards to safety, grade 1 and 2 adverse events were similar across all age groups. However, women greater than 65 experienced more grade 3 and grade 4 adverse events. Patients 70 years and older had less tolerability of the study drug compared to younger patients. Tolerability of therapy was defined as an adverse event leading to dose reductions or interruption, discontinuation of the study drug or a serious adverse event. In the patient group 70 years and older, 17% discontinued study drug secondary to an adverse event compared to 8% in the less than 65 year old group, and 77% in the 70 year and older group experienced an adverse event leading to dose reduction or interruption compared to 66% in the less than 65 year old group. More specifically, rates of neutropenia and hepatotoxicity were unchanged across the age groups, however, rates of infection, fatigue and diarrhea slightly increased with age.

The authors concluded that older patients receive benefit from initial therapy with a CDK 4/6 inhibitor in combination with an aromatase inhibitor as initial therapy for advanced or metastatic hormone receptor positive breast cancer. Both the severity of adverse events and the rates of dose modifications are higher in older women compared to women less than 65 years of age.

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[GS6-02] The benefit of amemaciclib in prognostic groups: An exploratory analysis of combined data from the MONARCH 2 and 3 studies

Dr. Goetz presented the exploratory analysis of the benefit of amemaciclib in different prognostic subgroups from combined data in the MONRACH 2 and 3 clinical trials. There are established pathologic and clinical features that predict activity of endocrine monotherapy in patients with advanced or metastatic breast cancer. More recently, the addition of CDK 4/6 inhibitors to endocrine therapy has been shown to improve progression free survival in patients with advanced or metastatic hormone receptor positive breast cancer. When to treat with dual CDK 4/6 inhibitor and endocrine therapy vs. endocrine monotherapy is an unanswered and clinically important question. This analysis combines data from two phase III studies of amemaciclib in combination with endocrine therapy with the aim to identify possible features that may guide selection of monotherapy versus combined therapy.

Monarch 2 and 3 enrolled patient with hormone receptor positive, HER2 negative, advanced breast cancer. Monarch 2 evaluated patients with endocrine therapy resistance and randomized patients 2:1 to amemaciclib + fulvestrant versus fulvestrant + placebo. Monarch 3 was first line therapy in the metastatic setting and randomized patients 2:1 to amemaciclib + an aromatase inhibitor versus and aromatase inhibitor + placebo. The results of these two studies have been published with Monarch 2 showing an increased PFS of 16.4 months in the amemaciclib groups vs. 9.2 months in the placebo group. Monarch 3 reported a PFS that is not yet reached in the amemaciclib arm versus 14.7 in the placebo arm.

For this analysis, a starting group of eleven variables including patient demographics, tumor biology and sites of metastatic disease were evaluated by analysis of PFS based on a univariate cox model. This process selected seven variables that were then evaluated in a stepwise fashion based on a multivariate cox model. This multistep process identified five variable that remained significant: performance status, tumor grade, progesterone status, presence of liver metastases and bone only metastases. In addition, a benefit with the addition of amemaciclib was observed in patients with a treatment free interval of less than 36 months.

The authors concluded that this exploratory analysis of over 1,000 patients treated on monarch 2 and 3 demonstrated that while all subgroups benefited from amemaciclib, patient that benefited the most from the addition of amemaciclib to endocrine therapy were those with good performance status, progesterone receptor negative tumors, high grade tumors, metastatic disease to the liver, bone only metastatic disease and those with a short treatment free interval.

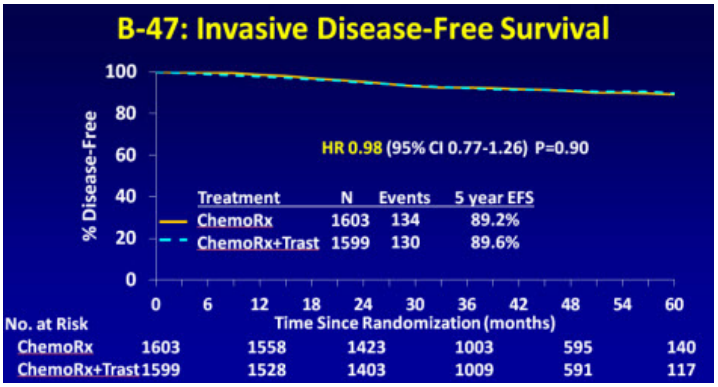
HER2 positive

[GS1-02] NSABP B-47 (NRG oncology): Phase III randomized trial comparing adjuvant chemotherapy with adriamycin (A) and cyclophosphamide (C) → weekly paclitaxel (WP), or docetaxel (T) and C with or without a year of trastuzumab (H) in women with node-positive or high-risk node-negative invasive breast cancer (IBC) expressing HER2 staining intensity of IHC 1+ or 2+ with negative FISH (HER2-Low IBC)

The first results of the NSABP B-47 trial were presented in the opening general session. This trial aimed to evaluate the benefit of one year of adjuvant trastuzumab after standard chemotherapy with adriamycin and cyclophosphamide for four cycles followed by weekly paclitaxel for twelve weeks in patients with low HER2 expression as defined as negative for HER2 by FISH and with IHC staining of 1+ or 2+. This study was conducted based on important questions that arose from two previous clinical trials, NSABP-31 and N9831. The combined analysis of these trials were presented at ASCO in 2005 and showed the very significant benefit in disease free survival of about of 18% in the group receiving one year of adjuvant trastuzumab. The eligibility criteria for the study included a positive FISH for HER or an IHC score of 3+. HER2 testing was performed at local lab sites and a subsequent tissue sample was sent to NSABP for later confirmatory testing. In NSABP-31, central HER2 status was performed for quality measures, and a large number of patients were found to be FISH negative (19.5%) and IHC 0-2+ (23.1%) or both (16.4%). Thus, an amendment was enacted requiring central HER2 testing which subsequently decreased the number of HER2 negative patients enrolled, but there was still an overall high number of patients enrolled with FISH negative tumor (11.5%) and IHC 0-2+ (16.7%). These patients were subsequently labeled as "HER2 low". Surprisingly, the subset analysis of the FISH negative and IHC <3 group showed a less than 0.5 hazard ratio for benefit from trastuzumab for disease free survival. The N9831 trial had patients that were also HER2 low and showed similar results. Therefore, the NSABP-47 trial set forth to determine the benefit of adjuvant trastuzumab in patients with low HER2 expression.

B-47 randomized 3,270 patients over 50 months who were either high-risk node negative patients or node positive patients with a HER2 IHC score of 1+ or 2+. If the IHC was 2+, then FISH was required to be negative with a ratio of less than 2.0 and HER2 gene copy number less than 4 per nucleus. Patients could be treated with physician's choice of two standard adjuvant regimens: Docetaxel and Cyclophosphamide for 6 cycles or Adriamycin + cyclophosphamide follow by weekly paclitaxel. They were randomized 1:1 with group two also receiving one year of adjuvant trastuzumab. The primary endpoint was invasive disease-free survival.

With a median follow up of 46 months, there was no significant difference in invasive disease-free survival with the chemotherapy group being 89.2% and the chemotherapy + trastuzumab being 89.3% (p=0.90 and HR 0.98). Overall survival was also similar in both groups with the chemotherapy group being 96.2% and the chemotherapy + trastuzumab being 94.8% (p=0.14 and HR 1.33). There was no subgroup identified that benefited from trastuzumab. Therefore, the primary objective of improving invasive disease-free survival was not meet, and the current practice of selecting patients with a FISH ratio of at least 2.0 or IHC 3+ for HER2 directed therapy should remain standard of care.



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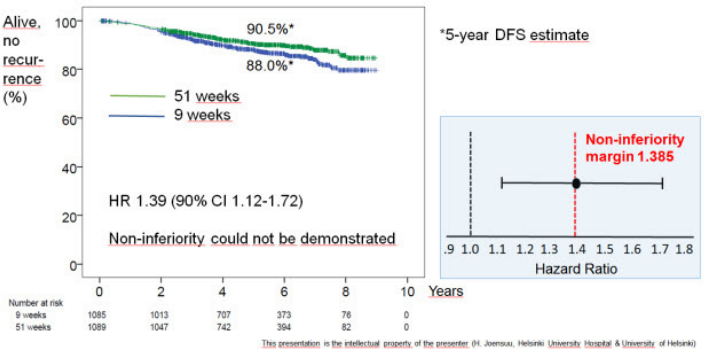
[GS3-04] A randomized phase III study of adjuvant trastuzumab for a duration of 9 weeks versus 1 year, combined with adjuvant taxane-anthracycline chemotherapy, for early HER2-positive breast cancer (the SOLD study)

The current standard adjuvant therapy for patients with early HER2+ breast cancer is trastuzumab based chemotherapy followed by adjuvant trastuzumab as a single agent to complete one total year of therapy. The SOLD trial sought to evaluate if a shorter duration of trastuzumab was non-inferior to the standard one year of trastuzumab. In SOLD, both groups received the same chemotherapy of docetaxel every three weeks with weekly trastuzumab follow by FEC for three cycles. Then half the patients received 14 dose of trastuzumab every three weeks to complete one year of total therapy, and the other group did not receive any additional trastuzumab. Both groups were treated with locoregional radiation therapy in accordance with local practice and hormonal therapy if hormone receptor positive. The primary objective was disease free survival (DFS) and secondary objectives included distant disease free survival, overall survival and safety. The patients included had node positive disease or if node negative, tumor sizes of greater than 5 mm. Patients with negative nodes and tumors less than 10 mm were required to be grade 2 or 3.

Accrual spanned 7 years and included 2,176 patients from 65 centers located in 7 different countries. The median follow up at the time of this data analysis was 5.2 years. Sixty percent of patients in both groups had node negative cancer. Disease free survival in the one year group was 90.5% compared to 88.0% in the 9 week group (HR 1.39 with 90% CI 1.12-1.72) and thus non-inferiority for short course of treatment with trastuzumab could not be demonstrated. Overall survival was high in both groups, but higher in the one year group at 95.9% compared to 94.7% in the 9 week group (HR 1.36 with 90% CI of 0.98-1.89). Cardiac toxicities were higher in the one

year trastuzumab group at 3.9% compared to 2.0 % in the nine week trastuzumab group. Also, congestive heart failure was more common in the longer duration group at 3.3% vs 2.9% in the nine week group. The authors thus concluded that adjuvant trastuzumab to complete one year of total therapy should remain the standard of care for this patient population.

Disease-free survival



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Early clinical trials

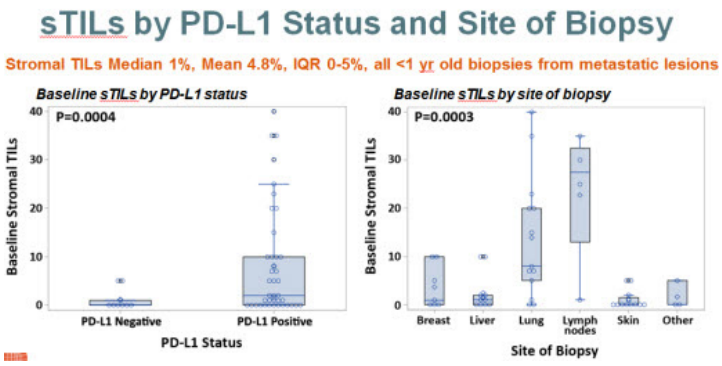
[GS2-06] Phase Ib/II study evaluating safety and efficacy of pembrolizumab and trastuzumab in patients with trastuzumab-resistant HER2-positive metastatic breast cancer: Results from the PANACEA (IBCSG 45-13/ KEYNOTE-014) study

There are multiple clinical and preclinical findings to suggest that the efficacy of trastuzumab could be enhanced by the addition of immune based therapies. This includes the observation of high T-cell infiltration in HER2+ positive breast cancers, TILs improving response to trastuzumab, an immune mediated component of its mechanism of action, and checkpoint inhibition in overcoming resistant to trastuzumab. Dr. Sherene Loi presented the results of the PANACEA trial which is a Phase 1b/II study evaluating the safety and efficacy of pembrolizumab and trastuzumab in patients with trastuzumab resistant HER2-positve advanced breast cancers. The phase 1b was conducted to determine the recommended dose of pembrolizumab in combination with standard trastuzumab dosing, and a phase II was completed to evaluate the efficacy and safety of this combination in PD-L1 expressing patients with advanced breast cancer who have progressed on trastuzumab-based therapy. A secondary endpoint of the study was to determine efficacy of trastuzumab and pembrolizumab in PD-L1 negative patients in the same clinical setting. An exploratory aim was to explore efficacy results by baseline stromal TIL level.

PANACEA was a single arm study conducted in two cohorts: one with PD-L1 positive patients and one arm with PD-L1 negative patients. In the phase II study, pembrolizumab was given as a dose of 200mg IV with standard every three week trastuzumab dosing. A total of 46 patients were enrolled in the PDL-1 cohort and 12 patients in the PD-L1 negative cohort. There were no cardiac events reports and no dose limiting toxicities in the phase 1b component. Immune related adverse events (AE) were common with 19% experiencing any grade immune related AE and 6 patients or 10% experiencing a grade 3 immune related AE. Four patients discontinued treatment secondary to an immune related AE. Of the immune related AEs, the most common were thyroid dysfunction and pneumonitis.

The study reached the primary endpoint with the desired number of pre-specified responders. The objective response rate in the PD-L1 positive cohort was 15.2%, and disease control rate was 24%. Some patients showed durable responses with a median duration of disease control of 11.1 months and five patients (10.8%) continuing on treatment with no progression at the time of this presentation. Importantly, in the PD-L1 negative cohort, there were no responses observed. The investigators found that higher stromal TILs was associated with a better response to trastuzumab and pembrolizumab and higher level of baseline stromal TILs in the metastatic site was associated with a higher disease control rate. A TIL level of as little of 5% was predictive of increased overall response rates (39%) and disease control rate (47%). Overall, this study

meet its primary endpoint of an overall response rate of 15% and disease control rate of 25% in the PD-L1 positive cohort. For responders, this combination can offer durable control of their cancer without chemotherapy.



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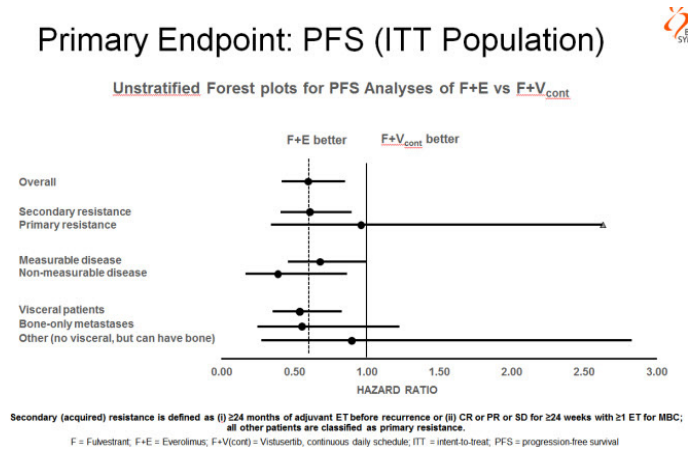
[GS2-07] MANTA - A randomized phase II study of fulvestrant in combination with the dual mTOR inhibitor AZD2014 or everolimus or fulvestrant alone in estrogen receptor-positive advanced or metastatic breast cancer

Dr. Peter Schmid presented the results of the MANTA trial which was a randomized phase II study with a new dual mTOR inhibitor AZD2014 (vistusertib). This was a four armed randomized clinical trial that was designed to test the impact of AZD2014 in comparison to fulvestrant alone or fulvestrant in combination with everolimus. Previous trials have shown substantial benefit of adding everolimus, which is an inhibitor to mTORC1 alone, to endocrine therapy in women with advance hormone receptor positive breast cancer. The clinical concern is that single inhibition of mTORC1 alone can lead to an unfavorable feedback mechanism through the AKT signaling pathway that results in resistance and cancer progression. Vistusertib differs from everolimus in that it is a dual inhibitor of both mTORC1 and mTORC2 and it demonstrated superior activity to everolimus in some preclinical models.

The main objective of this study was to evaluate if vistusertib when added to fulvestrant increased progression free survival (PFS) in comparison to fulvestrant alone or fulvestrant with everolimus. Two dosing schedules of vistusertib, continuous vs. intermittent, were evaluated as a secondary endpoint. A total of 333 patients were enrolled with the follow characteristics: estrogen receptor positive, HER2 negative, advanced breast cancer who had relapsed on or within 12 months from an adjuvant aromatase inhibitor or progression in the advanced setting while on an aromatase inhibitor. A maximum of one line of chemotherapy in the advanced setting was allowed. In regards to toxicities, there were more toxicities in the combination arms compared to fulvestrant alone. The intermittent high dose vistusertib group experience more nausea and vomiting compared to the continuous dose vistusertib group. The groups receiving everolimus or continuous vistusertib had higher rates of rash and stomatitis.

The results showed that the arm with fulvestrant and everolimus had the best PFS at 12.3 months compared with 8.0 months with the fulvestrant + vistusertib continuous dosing and 7.6 months with the fulvestrant + vistusertib intermittent dosing schedule. In the subset analysis, there was no group identified that benefit more from vistusertib compared to fulvestrant + everolimus. The authors thus concluded that the combination of everolimus + fulvestrant demonstrated improved PFS when compared to either schedule dose of fulvestrant + vistusertib. In an intent to treat population, the addition of vistusertib to fulvestrant alone did not show a significant disease free survival.



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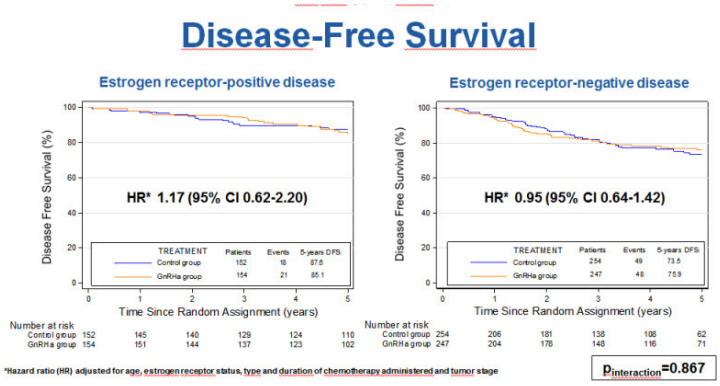
Survivorship

[GS4-01] Pooled analysis of five randomized trials investigating temporary ovarian suppression with gonadotropin-releasing hormone analogs during chemotherapy as a strategy to preserve ovarian function and fertility in premenopausal early breast cancer patients

Dr. Lambertini presented the pooled data of five clinical trials that examine the rate ovarian function preservation in women receiving gonadotropin-releasing hormone analogs during their chemotherapy treatments. For young women with breast cancer, fertility preservation is an area of concern. One option for fertility preservation is oocyte/embryo cryopreservation, but this does not prevent the harm from early ovarian failure in these young women. Several randomized clinical trials have utilized temporary ovarian suppression with gonadotropin-releasing hormone analogs (GnRHa) in an attempt to preserve both ovarian function and fertility. However, the data of these trials has been mixed. This study aimed to investigate the role of temporary ovarian suppression with GnRHa during chemotherapy in young women with early breast cancer via a systemic review and meta-analysis of available trials. Out of 13 randomized trials, five trials met the study inclusion criteria, 3 positive trials and 2 negative trials, with individual data for 873 patients equally divided between those receiving a GnRHa versus a control group.

The primary endpoints were premature ovarian insufficiency (POI) rate and post-treatment pregnancy rates. Secondary endpoints included amenorrhea rates one and two years after the completion of chemotherapy, disease-free survival (DFS) and overall survival (OS). The median age was 38 years old, about 40% were estrogen receptor positive and about half received anthracycline and taxane based chemotherapy. The POI rate as 14.1% in the GnRHa group compared to 30.9% in the control group with an OR of 0.38 and p<0.001. The subgroup analysis favored GnRHa treatment in all of the predefined groups. The amenorrhea rates were similar after one year, but the two groups diverged at two years with the GnRHa having 18.2% rate of amenorrhea compared to 30.0% in the control group. In regards to post treatment pregnancy rates, 10.% of women became pregnant in the GnRHa group versus 5.5% in the control group with an incident rate ratio of 1.83 which was statistically significant (p=0.03). All pregnancies were observed with estrogen receptor negative tumors in women less than 40 years or age. Disease free survival and overall survival were the same in both groups with a median 5 year follow up. This was true for both the estrogen receptor positive and negative groups.

The authors concluded that administration of GnRHa during chemotherapy was associated with a significant reduction in the risk of POI. The rate of post treatment pregnancy was higher in the group that received a GnRHa. Similar DFS and OS were observed in both groups regardless of the estrogen receptor status of the tumor. Based on this meta-analysis, they argue that a GnRHa should be considered standard of care for young women with early breast cancer as a means to decrease POI, and increase post treatment pregnancy rates.



[GS4-04] Randomized blinded sham- and waitlist-controlled trial of acupuncture for joint symptoms related to aromatase inhibitors in women with early stage breast cancer (S1200)

Aromatase inhibitors (AI) are an effective treatment for women with hormone receptor positive breast cancer and can significantly decrease the risk of recurrence. However, compliance secondary to side effects is a large contributing factor to non-compliance with AIs. One particular concerning side effect of AIs is arthralgias, and a handful of small studies have suggested that acupuncture may be beneficial in the treatment of AI associate arthralgias while other studies have showed no benefit. The interpretation of these studies has been difficult secondary to the short duration, small sample size, and non-standardized methods of the intervention. Therefore, this trial was designed to evaluate the effect of acupuncture on AI associate arthralgias in a blinded and randomized clinical trial with real acupuncture compared to sham acupuncture. These two groups were also compared to a waitlisted group which served as a control group.

This study randomized 226 women 1:1:1 to three arms: true acupuncture, sham acupuncture, and waitlist control. Both acupuncture groups received the procedure twice weekly for 6 weeks and then once weekly for an additional 6 weeks. All patients received acupuncture at the conclusion of the study. Assessments were taken at baseline, at 6 weeks, at 12 weeks and at 24 weeks. The primary outcome measure was brief pain inventory (BPI) worst pain score at 6 weeks. The investigators hypothesized that true acupuncture would decrease the worse pain compared to both sham acupuncture or wait listed controls. Eligible patients included women with stage 1-3 hormone receptor positive breast cancer who had been on treatment with a third generation AI for at least 30 days prior to registration with arthralgias that started or increased after starting an AI. A worse pain score on the BPI of 3 of more at baseline was required for entry. Patients could not have previously been on opioids, steroids or alternative physical therapy for AI induced arthralgias within 28 days of enrollment and no prior acupuncture for any joint symptoms was allowed.

The invention of true acupuncture was Standard Traditional Chinese Medicine point prescription to reduce pain and decrease stress and included the full body with auricular and joint-specific acupuncture directed to the most painful joints. In contrast, sham acupuncture was a shallow needle insertion using thin and short needles at non- acupuncture points. Wait listed controls received true acupuncture at week 24. A significant difference was observed in the change in the worse pain score in the true acupuncture group compared to both the sham acupuncture group and the waitlisted control group. There was no difference in the baseline and 6 week measurement on worse pain score in the sham acupuncture and the waitlist control groups. The study authors defined a significant change in pain score as a change of 2 points, and 58% of patients in the true acupuncture group had a drop in their pain score of at least 2 points compared to 31% in sham acupuncture and 30% in waitlist control. True acupuncture had an increase rate of bruising. The authors concluded that this study supports the use of acupuncture for AI-associated arthralgias.

ADVERSE EVENTS

	True Acupuncture (n=106) Grade				Sham Acupuncture (n=55) Grade			
ADVERSE EVENTS	0	1	2	3	0	1	2	3
Bruising	56	50	0	0	41	14	0	0
Dizziness	101	5	0	0	55	0	0	0
Ear pain	105	1	0	0	54	1	0	0
Hematoma	105	1	0	0	55	0	0	0
Bleeding at injection site	103	3	0	0	53	2	0	0
Pain in extremity	105	1	0	0	55	0	0	0
Presyncope	105	0	1	0	54	0	1	0

Grade 1 bruising (47% vs. 25%) p=.01

- Patients on true acupuncture were more likely to believe they were receiving true acupuncture 6 weeks (68% vs. 36%, p<.0001).
- The intervention effect did not differ between those believing vs. not believing they were receiving true acupuncture at either 6 weeks (p=.16) using interaction tests.

[GS5-07] Weight change in postmenopausal women and breast cancer risk in the Women›s Health Initiative Observational study

Dr. Chlebowski presented the data on weight change in postmenopausal women and its relation to breast cancer recurrence in the Women's Health Initiative (WHI) Observational Study. While breast cancer risk in postmenopausal women has been established in previous studies, the effect of weight loss on the risk of breast cancer recurrence is uncertain based on previous trials. This study sought to evaluate the association between weight change and breast cancer incidence as well as weight loss "intentionality" and breast cancer incidence. The WHI Observational study included over 93,000 postmenopausal women ranging in age from 50-79 years recruited from 40 US clinical centers between 1993-1998. As of September 2015, there was a mean of 11.4 years of follow up. Data collected included demographics, medical history and breast cancer risk factors collect by baseline questionnaires, medication review and mammogram data was collected if they were performed. Of the study group, 61,335 were deemed appropriate for this analysis. Incomplete data was the major reason for censoring patients from this analysis.

Height and weight at baseline and at year 3 was collect for BMI measurement. Three categories were set for weight change: 5% or less increase or decrease, more than 5% increase, and more than 5% decrease. Participants were also asked at year three if their weight had changed by 5 or more pounds in the previous two years and if that weight change was intentional or unintentional. Breast cancer ascertainment was completed through yearly contact with participants and subsequently confirmed after medical record review. Immunohistochemical information for hormonal status and HER2 status was obtained by review of local laboratory reports. Compared to women with stable weight, women who had a more than 5% increase in weight were more likely to be younger, Black and heavier smokers. Conversely, women with a more than 5% decrease in their weight were more likely to have higher BMI's, less physical activity and less likely to use supplemental hormonal therapy. In a multivariable analyses compared to the 41,139 women with stable weight, women with a 5% or greater weight loss (n=8,175) had a significantly lower breast cancer incidence with a HR of 0.88 and a p=0.02. Adjusting for mammography frequency did not change these findings. Women who had a 5% or greater gain in weight did not have a higher overall breast cancer incidence but did have a higher incidence of triple negative breast cancer. The intentionality of the weight change did not alter the findings. The authors concluded that this large prospective clinical study supports that decreasing weight by at least 5% in postmenopausal women can significantly decrease the risk of breast cancer and interventions in the group designed to generate weight loss may decrease the incidence of breast cancer.