analyzed for ESR1 mutations by next generation sequencing. The primary objective was to assess the progression-free survival (PFS) rate at six months. We applied a two-stage design with α=0.05, β=0.20, P0=0.4 and P1=0.75 was applied, requiring at least 8 of 14 ESR1 mutant patients to be free of progression at 6 months on paclitaxel/bevacizumab. For P0, we assumed a 6-months PFS rate of 40% on fulvestrant, which is a commonly used treatment in these patients. Secondary outcomes were objective response rate (ORR) and overall survival (OS).

Results: ESR1 mutations were detected in 20 (45%) baseline samples. The 6-month PFS rate was 83% for ESR1 wild-type patients versus 85% for ESR1 mutant patients (17/20). The median PFS was 8.6 months [95% confidence interval (CI), 8.2-9.1] for ESR1 wild-type patients versus 8.1 months [95% CI, 7.2-9.0] for ESR1 mutant patients [log rank P=0.807]. The ORR was higher in ESR1 wild-type patients than in ESR1 mutant patients [75% vs 50%] although this percentage was not significant [P=0.052]. The median OS was 24.8 months [95% confidence interval (CI), 17.4-32.2] for ESR1 wild-type patients versus 20.7 months [95% CI, 2.1-39.3] for ESR1 mutant patients [log rank P=0.443].

Conclusions: This explorative study indicates that in advanced breast cancer patients with ESR1 mutations in plasma it is worthwhile to start bevacizumab/paclitaxel as further treatment.

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30P Expression signature of Let-7a, miR-34a and miR-486-5p in young triple-negative breast cancer patients overexpressing PDL1: A step towards precision immuno-oncology

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Background: In an era of immunotherapeutic approaches, immune checkpoint blockers (ICBs) have revolutionised the oncology market. Yet, most patients do not benefit. The new direction has shifted towards identifying novel predictive biomarkers in the field of precision immuno-oncology. Thus, the development of a multifactorial synergistic predictive-model has become a pressing need. Triple-negative breast cancer (TNBC) and especially at younger age (<40 years) tends to exhibit an aggressive phenotype evading immune surveillance mediated by immune cells. This occurs by overexpressing PDL1 and shedding of CD155. Our group has recently identified sONE, a tumor suppressor lncRNA that is absent in young TNBC patients. sONE functional activity was found to be directly correlated to other immunomodulatory microRNAs. However, their expression signature in young TNBC patients has never been investigated. The aim of this study was to identify an immunomodulatory-related miRNA signature for young TNBC patients.

Methods: TNBC patients (n=28) were recruited. Median age at the time of diagnosis was 39 years old (range 22-70). Lymph node metastasis was evident in 60.7%. High Ki-67 (>15) was observed in 71%. Stage 3 diagnosis was evident in 53.6 %of patients. Almost 93% of tumors were invasive ductal carcinoma (IDC) and the rest were invasive lobular carcinoma (ILC). Tumor size >5 cm was recorded in 68%. RNA was extracted from tissues and serum, reverse transcribed and quantified using q-RT-PCR. TNBC cell lines were cultured, transfected using oligonucleotides using lipofection.

Results: An elevated expression pattern for PDL1 in young TNBC patients and a marked repression of CD155, let-7a, miR-34a and miR-486-5p compared to the older group were observed. Ectopic expression of let-7a and miR-34a resulted in a significant repression of PDL1 while miR-486-5p mimics resulted in an induction of CD155 levels. Such an immuno-modulatory miRNAs expression pattern was inversely correlated with tumor size and Ki-67 in TNBC patients. Yet, PDL1 was directly associated with lymph node metastasis and stage of disease.

Conclusions: This study identified a panel of three immunomodulatory miRNAs as a signature among young TNBC patients overexpresing PDL1 and underexpressing CD155.

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31P Association between breast cancer protein truncating variants and febrile neutropenia breast cancer patients treated with taxane or anthracycline chemotherapy in Singapore

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Background: Febrile neutropenia (FN) incidence across taxane or anthracycline chemotherapy regimens (T/AC) for breast cancer (BC) is high. BC patients (BCp) with FN face higher susceptibility to sepsis and other life-threatening infections, with FN-related mortality rate in BCp at 2-6%. Cancer susceptibility genetic variants can amplify chemotherapy-induced cytotoxicity that result in FN onset. We studied the association between carriership of protein truncating variants (PTV) in 34 BC predisposition genes and FN in T/AC-treated BCp.

Methods: Targeted sequencing (Fludigm Juno 192.48, Illumina Hiseq4000) was performed for 1,596 adult BCp with invasive BC (median age=52 years) treated with adjuvant/neoadjuvant T/AC (2000-2016). Genes known or suspected to predispose BC, including genes on commercial panels for predicting BC risk, were analysed: ABRAXAS1, AKT1, ATM, BABAM2, BARD1, BRCA1, BRCA2, BRIP1, CDHT, CHEK2, EPCAM, FANCC, FANCM, GEN1, MEN1, MLH1, MRE11, MSH2, MSH6, MUTYH, NBN, NF1, PALB2, PIK3CA, PMS2, PTEN, RAD50, RAD51C, RAD51D, RECQL, RINT1, STK11, TP53 and XRCC2. 441 BCp who received granulocyte-colony stimulating factor ≤30 days before or during T/AC were excluded. PTVs (frameshift/nonsense mutations or splice sites) were identified and collapsed into a binary variable. Association between PTV carriership (PTVship) and FN was analysed with logistic regression model; single gene PTVship associations were analysed with Fisher's exact test.

Results: In 1,155 BCp studied, 9% were carriers of at least one PTV. PTVship was found to decrease FN risk (OR=0.27, 95%CI 0.11-0.68, p=0.005, adjusted by site, ethnicity, BMI and first 4 principal components). No single gene was found to be significantly associated with FN.

Conclusions: PTVship appears to be protective against FN. Other FN risk factors need to be considered in future studies.

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32P PIK3CA exon 9 and 20 mutations in early luminal breast cancer: Case series and review of the literature

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Background: PI3K/AKT/mTOR pathway is frequently altered in breast cancer. PIK3CA mutations have been described in up to 40% of luminal breast carcinomas. Mutations located in two hotspots in exons 9 and 20 (codons 545, 546 and 1074) account for more than 85% of all point mutations in this gene. PIK3CA alterations have been shown to be related with endocrine therapy resistance.

Methods: We have searched for mutations on PIK3CA exons 9 and 20 in a set of 166 luminal, treatment naive, breast cancer cases. DNA was extracted from paraffin embedded tissue from the primary tumor. We used a previously published pyrosequencing protocol by Nosho et al (Neoplasia, 2008). We reviewed current literature on early breast cancer and sistemic therapy resistance.

Results: 26.5% (44 samples) of all the cases in our serie was mutant for either exons 9 or 20. Mutation distribution showed codon 1074, exon 20, as the most frequently mutated (16.87%). H1047R was the most common change seen. PIK3CA mutations have been commonly considered an adquired resistance mechanism to endocrine therapy. Its importance on early breast cancer development and treatment selection has not been deeply explored.