Methods: Our study included 101 HER2-positive early BC patients treated with adjuvant RT, chemotherapy, and trastuzumab. We isolated DNA from buccal swabs and genotyped all patients for CAT rs1001179, GSTP1 rs1138272, GSTP1 rs1695, SOD2 rs4880, PON1 rs854560, and PON1 rs662 polymorphisms using competitive allele-specific PCR. Association of polymorphisms and clinical parameters with skin RT adverse events was evaluated using logistic regression.

Results: Median follow-up after RT was 4.0 (2.6–5.4) years. Patients received either 2S × 2 Gy (84, 83.2%) or 17/18 × 2.5 Gy (17, 16.8%) of total radiation dose. Among all, 58 (57.4%) patients received taxanes, and 29 (28.7%) patients had arterial hypertension (AH). In total, 33 (32.7%) patients experienced grade ≥2 late adverse events according to LENT-SOMA criteria, and 12 (11.9%) grade 2 skin toxicity according to CTC criteria. Patients with AH and patients receiving treatment with taxanes were significantly more likely to experience grade 2 skin toxicity (P = 0.016 and P = 0.012, respectively) or grade ≥2 late adverse events (P < 0.001 and P = 0.001, respectively). RT scheme was not associated with skin adverse events. Late adverse events were significantly more common in carriers of at least one polymorphic PON1 rs854560 allele (OR = 3.03; 95% CI = 1.07–8.53, P = 0.036) and carriers of at least one polymorphic CAT rs1001179 allele (OR = 2.71; 95% CI = 1.60–7.33, P = 0.049) after adjustment for clinical variables.

Conclusion(s): HER2-positive BC patients with AH, treated with taxanes and adjuvant RT, had significantly more late skin adverse events than patients without these factors. The PM-ISR approach was applied for return of results to at-risk individuals. No significant relationships.

P116 Predicting clinical behaviour of breast phyllodes tumors: utility of Singapore nomogram

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Goals: Phyllodes tumor (PT) is an uncommon fibroepithelial neoplasm that constitute approximately 0.3%–1% of primary breast tumors. The reproducibility of grading has long been challenging as established histological features can be weighed differently by individual pathologist. This interpretive subjectivity has made it difficult to accurately categorize it benign, borderline or malignant subtypes. In an attempt to predict the clinical behavior of phyllodes tumor, Tan et al in 2011 introduced the Singapore nomogram (SN) by using histological parameters- degree of stromal atypia, stromal mitotic count, presence or absence of stromal overgrowth and surgical margin status (AMOS criteria). Due to suboptimal correlation between histological classification and clinical behavior, we here explore the utility of nomogram for predicting the recurrence free survival.

Methods: Hospital records of PT cases treated at Kidwai Memorial Institute of Oncology, Bangalore, India from 2001 to 2012 were analyzed. They were stratified into benign, borderline and malignant grades based on histological parameters and SN score was calculated according to AMOS criteria. Kaplan-Meier survival curves were used to estimate Recurrence free survival (RFS), which was defined as the time from the date of surgery to the date of first relapse or death from PT or to the last follow-up date for censored cases. Statistical analysis was performed to evaluate the effects of individual predictors in the SN as well as of final nomogram score and histological score on RFS. Harrel’s c-index was calculated to evaluate the concordance between predicted and observed responses of individual subjects in terms of the SN and the total histological score separately.

Results: One hundred sixty two patients were included in the final analyses. Histologically, there were 95(59%) benign, 29(18%) borderline and 38(23%) malignant PT. Recurrences were noted in 31(19%) cases. All the four parameters of AMOS criteria significantly affected the RFS on univariate analysis. Cox regression also revealed that high SN and histological score both predicts high risk of relapse. However, the concordance index was higher for SN score (0.92) when compared with histological score (0.78).

Conclusion(s): The Singapore nomogram is useful in predicting outcome in PT and can be applied for patient counselling.

Conflict of Interest: No significant relationships.

P117 Implementation of a pathology-supported genetic testing framework for return of research results to family members of deceased breast cancer patients with somatic TP53 variants

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Goals: Accurate estimation of cancer risk in families of deceased patients with deleterious variants in high-risk genes such as BRCA1/2 and TP53 known to contribute causally to tumour type, is hampered by lack of stored DNA for cascade testing. To allow extended genetic testing and data sharing in eligible cases, we developed a pathology-supported genetic testing (PGST) framework for application of personalised medicine, using an integrated service and research (PM-ISR) approach. This enables long-term sample storage with the goal to integrate germline and tumour genetic testing across illness and wellness domains.

Results: Our study included 101 HER2-positive early BC patients treated with adjuvant RT, chemotherapy, and trastuzumab. We

Methods: The study cohort includes two deceased breast cancer patients selected from a genomics database of over 160 cases subjected to next generation sequencing (NGS) of tumour DNA. These patients diagnosed with breast cancer at the ages of 40 years (Case 1) and 31 years (Case 2) previously tested positive for the TP53 c.384delC (p.P128fs*42) and c.818G>A (p.R273H) variants, respectively. The PM-ISR approach was applied for return of results to at-risk

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family members following a request for use of their stored DNA for confirmation or exclusion of the familial risk associated with Li-Fraumeni Syndrome. Eligibility assessment was based on written informed consent, indicating approval by the deceased patients for storage of germline DNA. This enabled further testing using whole exome sequencing (WES) on behalf of at-risk family members.

Results: The TP53 variants were excluded in the germline DNA of both breast cancer patients. Review of the histopathology and immunohistochemistry reports provided insight into the drug response reported. A strong family history of cancer was reported in Case 2, for whom an adaptive WES report was generated for genetic counselling of at-risk family members, using the PGCT framework.

Conclusion(s): The clinical utility of PSCT beyond the lifespan of a TP53 variant carrier was demonstrated for the first time, which highlighted the value of a dynamic informed consent process rather than a once-off event. The WES results provided to at-risk family members of the deceased breast cancer patients clarified the familial risk as the primary concern. TP53 variants occurred in the tumour cells only, therefore there was no risk of Li-Fraumeni syndrome in the family based on the variants excluded in germline DNA. We conclude that germline testing should always be offered when a TP53 variant is detected in tumour DNA, irrespective of family history.

Conflict of Interest: No significant relationships.

PI110
The role of tumor-infiltrating lymphocytes, prognostic and predictive significance in breast cancer
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Goals: The immune system can have a significant impact on the prognosis as well as the performance of chemotherapy.

Methods: Using TMA we have shown a quantitative assessment of the subpopulation of CD4+, CD8+, FoxP3, CD8/FoxP3, PD-L1 of T-lymphocytes. In order to study the significance of the immunological aspects of the antitumor response, 638 cases were studied with regulatory genes-PD, PDL-1 and FOXP3 were studied. Of these, 281/633/548 patients were also tested for T-cell response markers CD3, CD4 (regulatory lymphocytes) and CD8 (cytotoxic).

Results: TILs were assessed in 1152 cases, of which 67% level was low, 25% moderate and 8% severe. Among the studied patients, 296 had a CD4+ percentage equal to or less than 50%. The 10-year overall survival rate of patients in this group reached 93%, which is considered a favorable group (p < 0.05) for early BC (stages T1-T2, N0). In 98 patients, the CD4+ percentage exceeded more than 50%. 10-year overall survival of patients was significantly lower than 82% (p < 0.05)(F2). There was no significant correlation between the degree of CD4+ lymphoid infiltration and disease-free survival rates (p = 0.27), although with a high CD4+ level (> 50%) of cases, 10-year overall survival rates decreased (F3).

The presence of FOXP3 expression in ER+ breast cancer on TILs is significantly associated with a trend towards a lower overall survival rate (p = 0.06). FoxP3-regulatory TILs are a poor prognostic indicator in ER+BC, but a favorable prognostic factor in HER2+ER-subtype BC. The predictive value of FOXP3 TILs differs depending on the expression and status of ER and HER2 and CD8+ T-cell infiltration (F5).

In the literature, particular importance is attached to the study of CD8+ and FOXP3, it is believed that the co-expression of these markers has prognostic value and depends on the status, especially in the ER+ and HER2+subgroups (F6).

Conclusion(s): The low degree TILs (0–10%) is observed in Luminal A subtype. About 80% of BC patients have low tumor infiltration rates of CD8+ cytotoxic T lymphocytes and CD3+ TILs. The level of infiltration of different types of T-lymphocytes does not depend on the size of the primary tumor. The PD-L1 gene is more often detected in TNBC, 1.5 times less often in HER2 + BC, and extremely rarely in luminal A subtype (F1). The simultaneous expression of PD, PD-L1, and FOXP3 is determined by aggressive tumor growth, found in 11.5% of pts. A high CD8+/FoxP3 ratio indicates a good prognosis of the disease. The percentage of CD4+ T-lymphocytes less than 50% indicates a good prognosis and a high ten-year survival rate. Severe (more than 10%) CD8+ lymphoid infiltration increases ten-year survival (80%) and overall survival (92%) in pts with pT1-2N0. Relapse-free ten-year survival rates were higher in the group without PD-L1 expression (70% versus 41%) in the presence of PDL-1 expression [p = 0.02](F4).

Conflict of Interest: No significant relationships.

PI119
The level of adherence to medical standards as a prognostic factor for breast cancer recurrence
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Goals: Breast cancer recurrences are among the leading causes of deaths related to this malignancy’s progression. Many experts have tried to create several clinical calculators, also known as nomograms, to predict treatment outcomes, survival, and to prognose recurrent disease. To these date, no analyses have reported the level of adherence to medical standards and their relation to the recurrence rate.

Methods: We retrospectively analysed data from 263 patients diagnosed and treated for local recurrence of breast cancer between January, 2012, and March, 2020, at two Bulgarian centers - National Hospital of Oncology and Lozenetz University Hospital. Primary breast cancers were treated in many different hospitals. The level of adherence to medical standards was assessed by 4a,10a,10b,11a,11b,12,13a, and 13b quality indicators (QIs) adopted by European Society of Breast Cancer Specialists (EUSOMA).

Results: The median age was 45.2 years at the time of first diagnosis. The time interval between the primary tumor and the recurrence was from 1 month to 36 years. 44.9% of patients had family history of breast cancer. The majority of primary tumors were in T1 stage - 68.82% (T1a – 1.5%, T1b – 49%, T1c – 18.3%), and only 0.8% of them were in T3. Regional lymph nodes could not be assessed (Nx) in 11.4% of patients with primary tumors, which leads to a significant decrease in level of adherence to medical standards in these patients. 67.3% of relapsing patients had high estrogen receptor (ER+) titers (>50%). We reported HER2-negative status in 79.8% of patients with the primary cancer and in 85.2% of relapsing patients. The level of adherence to medical standards is faintly 76.3% in primary tumors. The results include significant differences in the level of adherence to medical standards according to the patients’ age and clinical treatment, and can be used as prognostic factors.

Conclusion(s): Despite the many efforts that have been made in the quality of breast cancer care, it would be greatly improved if we reduce recurrences. Therefore, knowledge of the prognostic factors is key to a better prognosis. Monitoring the level of adherence to medical standards for breast cancer recurrence can aid in the development of treatment strategies and follow-up in these at-risk patients.

Conflict of Interest: No significant relationships.