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 25 × 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 effects of RT, especially if they were carriers of at least one polymorphic PON1 rs854560 allele or at least one polymorphic CAT rs1001179 allele. Polymorphisms in antioxidant genes could thus serve as predictive factors of RT late skin reaction.

Conflict of Interest: No significant relationships.

P116 Predicting clinical behaviour of breast phyllodes tumours: 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 into benign, borderline or malignant subtypes. In an attempt to predict the clinical behavior of phyllodes tumors, 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).

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.

MULTI-PLATFORM RESULT
Familial risk:  8 August 2020: WES did not identify any pathogenic, cancer-causing gene variants in this patient with a strong family history and early-onset breast cancer. Information on three variants of uncertain clinical significance (VUSs) identified in the BRCA1/2 and RET genes, and a low-penetrance pharmacogenetic TP53 variant is kept in a research database for future reference (available for annual reinterpretation)

Treatment:  4 March 2015: NGS previously performed on the residual primary tumour detected TP53 p.R273H (63%; actionable) and AURKA p.I158S (12%; VUS) in tumour DNA of the index case, which were excluded in germline DNA using WES. Taxane- and Anthracycline-based chemotherapy were identified as anti-cancer therapies with potential clinical benefit based on high TL3 and TOFJA expression, respectively. 15 August 2020: Initially, the tumour responded well to anthracyclines, but progressed on taxane-based chemotherapy. Unfortunately, no approved targeted therapies for TP53 variants are available, which is compatible with the chemotherapy resistance that was experienced during her cancer progression.

Comorbidities:  13 April 2015: Due to the iron deficiency anaemia documented at the time that the wellness screen was performed, WES analysis was extended to the entire TMPRSS6 gene, indicating heterozygosity rs855791, rs2543519 and rs2235324. Close relatives with a similar risk profile are advised to ensure optimal blood/serum iron status.

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.P128Leufs*42) and c.818G>A (p.R273H) variants, respectively. The PM-ISR approach was applied for return of results to at-risk