00245 Characteristics, Biomarker and mRNA Profiling in Metastatic Triple Negative Breast Cancer: Defining Predictors

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Aims: To evaluate immunohistochemical protein expression of biomarkers, to determine mRNA level of these proteins by NanoString Technology, and to correlate findings from immunohistochemistry and mRNA assays with clinical outcomes.

Methodology: The study cohort comprised 160 metastatic triple negative breast cancers (TNBCs) diagnosed at the Department of Anatomical Pathology, from 1994 to 2013. Pathologic parameters of tumour size, histologic grade, lymph node stage were reviewed. Immunohistochemistry was performed using antibodies to cancer stem cell markers (ALDH1A1, CD44, CD24), p53, androgen receptor, BRCA1, BRCA2, caveolin1, CXCR4, VEGF, Snail2, ID4, E-cadherin, FGFR1 and FGFR2 using tissue microarrays. Thirty seven tumours were subjected to mRNA profiling of these proteins using NanoString Technology. Overall survival (OS) and survival after metastasis were correlated with protein expression and mRNA assays.

Result: The age ranged from 25 to 87 years (mean 53, median 52). Majority (79%) were Chinese. Tumour size ranged from 0.5 to 19 cm (mean 4.4 cm, median 3.5 cm). T2 tumours were observed in 79% of patients. Grade 3 tumours predominated (77%). Node positivity occurred in 59% of cases. Follow-up ranged from 3 to 203 months (mean 44, median 32 months). Patients whose tumours harboured CD44 and p53 protein expression disclosed poorer OS (p=0.023 and p=0.039 respectively). CD44 protein expression predicted worse OS (HR1.534, 95%CI 1.016-2.316, p=0.042). Tumours with higher mRNA levels of ALDH1A1 showed worse OS (p<0.001) and survival after metastasis (p<0.001). These findings were supported by multivariate analysis (HR4.697, 95%CI 1.651-13.362, p=0.004 and HR 5.262, 95%CI 1.749-15.828, p=0.003 respectively).

Conclusion: Our study demonstrates that protein expression of CD44 and p53 in metastatic TNBCs is significantly associated with poorer outcome and CD44 protein is a predictor of OS. Higher ALDH1A1 mRNA levels predict both OS and survival after metastasis. Evaluation of cancer stem cell markers facilitates prognostic assessment and may provide new insights for further therapeutic paradigms.