

P20 QUANTITATIVE GENE EXPRESSION BY RT-PCR IN CLASSIC AND VARIANT LOBULAR CARCINOMA IN ER+ BREAST CANCER

Poster Abstracts I

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Goals: Classic lobular carcinoma is characterized by a distinctive morphology, loss of E-cadherin commonly due to mutation or deletion of CDH1 on chromosome 16q, and a variable clinical course (Pestalozzi J Clin Oncol. 2008; 26: 3006). Variants (pleomorphic, solid and alveolar) with distinct morphologies and potential differences in outcome have been described (Rosen 2009). Herein we provide an 8-year update of the patterns of quantitative gene expression as measured by the 21 gene Oncotype DX[®] assay observed between ductal NOS (DC) and classic and variant lobular carcinomas.

Methods: All tumors analyzed in the Genomic Health laboratory from 6/1/04–5/31/12 were included. Central path used WHO criteria for classification of classic lobular (CL), solid & alveolar lobular (SAL), and pleomorphic lobular (PL) carcinomas. Quantitative expression of 16 cancer related genes was measured on a scale from 2 to 15 (relative to reference genes) where a 1 unit increment is associated with an ~2-fold change in expression. Descriptive statistics for RS & individual genes [ER, PR, invasion gene group (IGG) & proliferation gene group (PGG)] among the different subtypes were obtained. Comparisons of means among the subtypes were adjusted to control the overall error rate under any complete or partial null hypothesis.

Histologic subtype	N	Low (<18)	Intermediate (18–30)	High (>31)	ER+/PR?
Classic lobular (CL)	20,844	60.8%	35.9%	3.3%	15.2%
Pleomorphic lobular (PL)	1,867	52.5%	39.8%	7.7%	19.4%
Solid/alveolar lobular (SAL)	1,231	58.0%	31.5%	10.5%	24.0%
All lobular	23,942	60.0%	36.0%	4.0%	16.0%
Ductal NOS (DC)	234,518	53.8%	33.3%	13.0%	14.1%

Results: DC accounted for 81.8% of 286,726 cases, CL 7.3%, SAL 0.4% and PL 0.4%. For all types a continuous range of RS was observed. DC had the greatest percentage of high risk RS followed by SAL, PL and CL. DC had the highest mean RS and PL and CL had the lowest RS. SAL had the highest mean ER expression and CL and PL had the lowest ER expression. These results may reflect a submission bias and are not population based. The proportion with ER+/PR?

phenotype was slightly different among the subtypes: SAL (24.0%) and PL (19.4%) had a higher incidence compared to DC (14.1%) and CL (15.2%). SAL had the highest PGG expression; CL had the lowest. DC had the highest IGG; CL had the lowest.

Conclusion: Classic lobular carcinoma and the lobular carcinoma variants are characterized by differential patterns of gene expression. Outlier cases are not infrequent within each of the special subtypes in this large observational cohort. The variation in gene expression, noted by histologic subtype, will be presented in detail. As an employee at Genomic Health, Inc., I am compensated with salary, benefits, and stock. I also have stock options as an employee of Genomic Health, Inc.