

2. Survival impact of HER-2/Neu, Cox-2, urokinase plasminogen activator (upa), cytokeratin 17/5,6 and other markers with long-term outcome of early breast cancer. Report from the British Columbia Tissue Micro-Array Project (BCTMAP)

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Tumor samples are available from over 19,600 Stage I-III breast cancer patients treated according to evolving British Columbia guidelines from 1978 to 1990. A tissue micro-array (TMA) was constructed from 930 of these patients, all of whom participated in randomized or phase II studies. Outcome was defined as 20-year Breast Cancer specific Survival (BrCaSS), with events defined as Breast Ca death. Follow up was median 17.8 years (ranges 11–28). Multiple tumor markers were tested, and results correlated with 20-year BrCaSS for markers expressed versus non-expressed.

20-year BrCaSS			
Marker	Expressed (%)	Not expressed (%)	p-Value
Her-2-IHC	34	48	<0.0001
Her-2 FISH	33	48	0.0004
Her-2 ACIS IHC**	32	47	0.0001
Cytokeratins 17/5,6 IHC:	35	47	<0.0020
uPA IHC	46	52	0.0300
Cox-2 IHC	32	45	0.0260

No difference in BrCaSS was found for aromatase, integrin-linked kinase (ILK), IGF-1 and Topo-isomerase-2. The negative predictive value of IHC versus FISH and ACIS-IHC versus FISH was 96 and 97%, respectively. The positive predictive value of IHC versus FISH and ACIS-IHC versus FISH was 84 and 84%, respectively. All tests, with the exception of HER-2 FISH were done by IHC. Results of other markers (VEGF, ER/PgR, hypoxia markers, etc.), and an interactive multivariate analysis adjusting for conventional prognostic factors and for all above markers, are in progress.

Conclusions 1. The TMA is a technique which provides opportunity for rapid screening of multiple genetic markers. 2. Expression of Her-2/Neu, uPA, Cox-2 and Cytokeratin 17/5,6 (but not of Aromatase, ILK, TOPO-II and IGF-1) is associated with inferior BrCaSS. 3. HER-2 determination by ACIS-IHC provides comparable results to IHC done manually (with a potential for more uniform reporting), and both provide comparable results to Her-2 assessment by FISH. **ACIS-IHC: IHC red by Automated Cell Image System (M.L.)