



Mammostrat™ as a tool to stratify patients at risk of recurrence during endocrine therapy.

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Objectives

To evaluate the prognostic value of a simple IHC test (Mammostrat™) using multiple immunohistochemical markers in early breast cancer.

Introduction

Patients with early stage, ER+ve breast cancer have excellent prognosis with approximately 90% 5 year disease free survival when treated with endocrine therapy. However, for patients who relapse during endocrine therapy additional adjuvant therapy options, such as chemotherapy, are clearly indicated. The challenge is to prospectively identify such patients. The Mammostrat® test comprises 5 simple immunohistochemical markers (p53, HTF9C, CEACAM5, NDRG1, SLC7A5) which stratify node negative patients on tamoxifen therapy into low, moderate and high risk groups. We have now tested the efficacy of this panel in a mixed population of node positive/node negative cases treated in a single centre (Edinburgh Breast Unit) with breast conserving surgery.

Materials & Methods

TMA's from a consecutive series (1981-98) of 1,812 women managed by wide local excision and postoperative radiotherapy (45Gy in 20-25 fractions) were collected following appropriate ethical review. Of 1390 cases stained, 197 received no adjuvant hormonal or chemotherapy, 1044 received tamoxifen only as adjuvant therapy and 149 received a combination of hormonal and chemotherapy. Median age at diagnosis was 57, 71% were post-menopausal, 23.9% node positive, median size was 1.5 cm. Samples were stained, using triplicate 0.6mm² TMA cores and positivity for p53, HTF9C, CEACAM5, NDRG1, SLC7A5 recorded as previously described. Each case was assigned a Mammostrat score and RFS and OS analysed by marker positivity and Mammostrat score.

Results

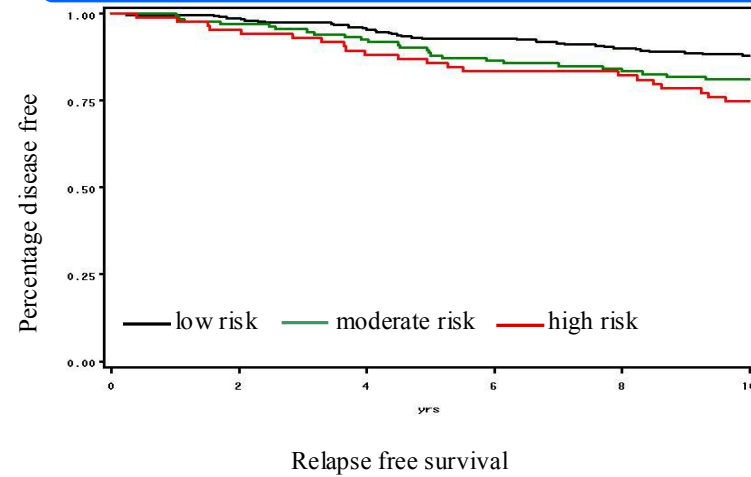


Figure 1: RFS by mammostrat score in 531 Node negative/ER positive patients treated with tamoxifen (see below)

Staining for all 5 antibodies was successful in 1174/1390 (84%) of cases. In the primary analysis of 531 N0/ER+ve Tamoxifen only treated patients Mammostrat was significantly associated with relapse free survival (RFS) in univariate (p=0.025; Figure 1 above) & multivariate proportional hazards analysis (p=0.01, HR=1.3, 95%CI. 1.08-1.74). PgR, multifocality and menopausal status were significant co-variables (p<0.05, HR 0.89, 2.0 & 0.6 respectively). The Nottingham prognostic index was non-significant.

Variable	P	Hazard	95%CI lower	95%CI upper
PgR	0.0058	0.897	0.831	0.969
Multifocality	0.0088	2.090	1.204	3.628
Menopausal status	0.0193	0.597	0.388	0.920
Mammostrat	0.0322	1.308	1.023	1.672
Path. size	0.0374	1.033	1.002	1.065

Table 1: Multivariate analysis in 531 Node negative/ER positive patients treated with tamoxifen (see above)

Results

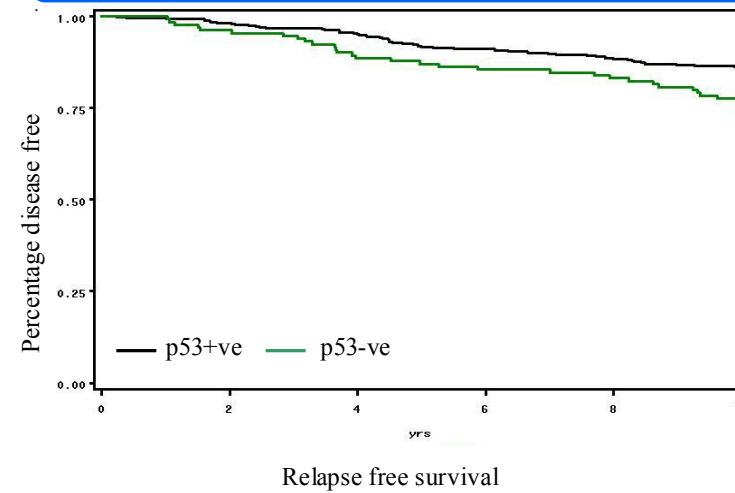


Figure 2: Of the 5 antibodies comprising the mammostrat panel, only p53 (p=0.04) was independently predictive of survival.

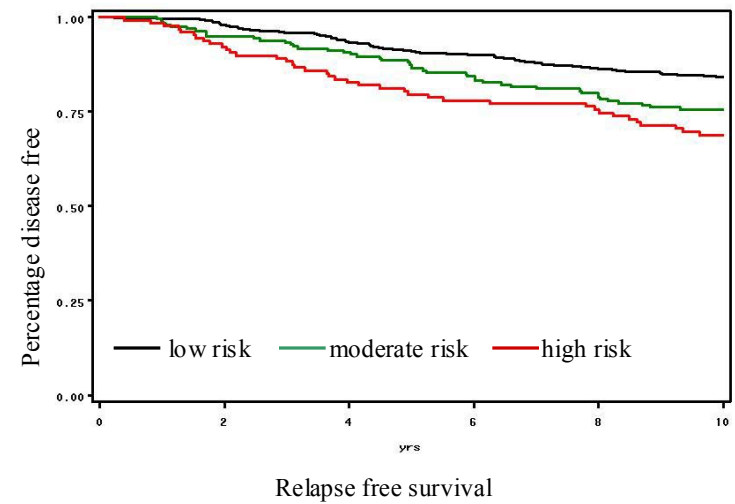


Figure 3: RFS by mammostrat score in 781 Node +/-ER positive patients treated with tamoxifen and chemo/tam.

Results

Variable	RFS	OS
Mammostrat	0.0039	0.0461
S0730	0.1927	0.9314
S0729	0.0513	0.0945
S0731	0.0179	0.0048
S5092	0.0696	0.1615
S5095	0.0164	0.6203

In a secondary univariate analysis of 781 patients (including N+ve and chemo/tam treated patients) Mammostrat was predictive of RFS & OS (p<0.01) with NDRG1/CEACAM5/p53 also predictive of RFS(p<0.05). However Mammostrat was not independent of nodal status, pathological size, grade or multifocality in a proportional hazards analysis.

Conclusions

In the Edinburgh BCS population Mammostrat was predictive of RFS (both local and distant relapses) in N-ve/ER+ve patients treated with tamoxifen alone irrespective of menopausal status. There was a strong correlation between Mammostrat scores and grade, however, in a multivariate analysis Mammostrat contributed significantly to prognostication along with PgR, multifocality, pathological size and menopausal status.

References

1. Ring,B.Z, Seitz,R.S, Beck,R, Shasteen,W.J, Tarr,S.M, Cheang,M.C.U, Yoder,B.J, Budd,G.T, Nielsen,T.O, Hicks,D.G, Estopinal,N.C, Ross,D.T. Novel prognostic immunohistochemical biomarker panel for estrogen receptor-positive breast cancer Journal of Clinical Oncology (2006) 24:3039-3047