2010年11月20日 NCCN/JCCNB Seminar in Japan 開催のお知らせ New 当日のプログラムを下記に掲載いたしました。

＜ テ ー マ ＞ 治療効果予測と予後予測～乳がんのターゲット治療の模索～
乳がんにおける予後及び治療効果の予測検査法について、欧・米・東アジアからの招聘者と共に検討する国際セミナーです。

＜ 場 所 ＞ 東京国際フォーラム ホールB5

The Current Status and the Future Prospects of Multigene testing in Europe

Emiel J. Rutgers

The Netherlands Cancer Institute
Antoni Van Leeuwenhoek Hospital
Amsterdam

NKI-AVL

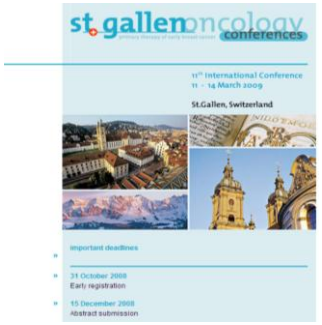
St. Gallen Recommendations 2009 = ‘Europe’ (?)

St Gallen Recommendations 2007 for Adjuvant Treatment

	Highly endocrine responsive	Incompletely endocrine responsive	Endocrine non-responsive
HER2-negative	**ET (consider adding CT according to risk)**	**ET (consider adding CT according to risk)**	**CT**
HER2-positive	**ET + Trastuzumab + CT**	**ET + Trastuzumab + CT**	**ET + Trastuzumab + CT**

endocrine highly and incompletely responsive HER2neg patients consider adding chemotherapy according to risk

ET: endocrine therapy
CT: chemotherapy



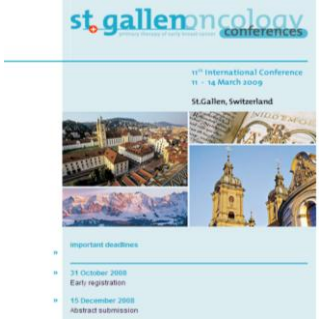
Goldhirsh et al, Ann Oncol 2007

Intermediate Risk Treatment Advice

	Highly endocrine responsive	Incompletely endocrine responsive	Endocrine non-responsive
HER2-negative	**ET** (consider adding CT according to risk)	**ET** (consider adding CT according to risk)	**CT**
HER2-positive	**ET + Trastuzumab + CT**	**ET + Trastuzumab + CT**	**ET + Trastuzumab + CT**

- St Gallen 2009:The panel accepts the use of validated molecular based tools, if readily available, as an adjunct to high quality standard histopathologic assessment in patients with ER+ breast cancer when the doctor and the patient are uncertain or ambivalent about the administration of adjuvant chemotherapy.

  Optimally the test should be used in clinical trials.



- Yes 80%
- No 18%
- unknown 3%

Guidelines: St Gallen International Expert Consensus 2009

Table 3. Chemoendocrine therapy in patients with ER-positive, HER2-negative disease

Clinicopathological Features			
	Relative Indications for Chemoendocrine therapy	**Factors Not Useful for Decision**	**Relative Indications for Endocrine Therapy Alone**
ER, PgR	Lower ER and PgR level		Higher ER and PgR level
Histological Grade	Grade 3	Grade 2	Grade 1
Proliferation	High[a]	Intermediate[a]	Low[a]
Nodes	Node positive (4 or more involved nodes)	Node positive (1-3 involved nodes)	Node negative
Peritumoral Vascular Invasion (PVI)	Presence of extensive PVI		Absence of extensive PVI
pT-size	> 5cm	2.1 – 5 cm	≤ 2cm
Patient Preference	Use all available treatments		Avoid side effects
Multi-gene Assays			
Gene Signature[b]	High score	Intermediate score	Low score

St. Gallen Recommendations on March 14th, 2009

MammaPrint Accepted into St. Gallen's Oncology Guidelines for Early Stage Breast Cancer Treatment

"The Panel accepts the use of validated molecularly based tools if readily available as an adjunct to high-quality standard histopathologic assessment in patients with ER+ breast cancer when the doctor and patient are uncertain or ambivalent about the administration of adjunctive chemotherapy."

In addition, the Panel felt "intermediate" results were of little clinical value.

St. Gallen Guideline Consensus, Annals of Oncology, 2009

Guidelines: St Gallen International Expert Consensus 2009

Table 3. Chemoendocrine therapy in patients with ER-positive, HER2-negative disease

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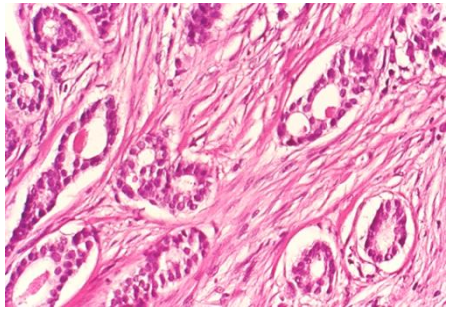
Patient Preference	Use all available treatments		Avoid side effects
Multi-gene Assays			
Gene Signature[b]	High score	Intermediate score	Low score

21 recurrence score

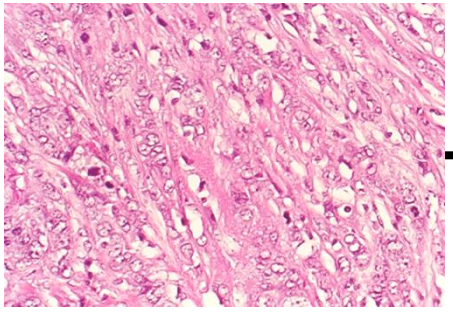
70 gene prognosis signature

Contrast of Appearance and Expression Phenotyping

Microscope

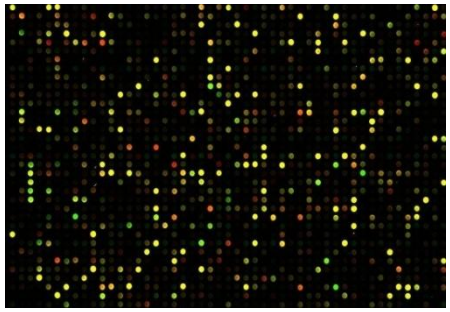


Low Grade

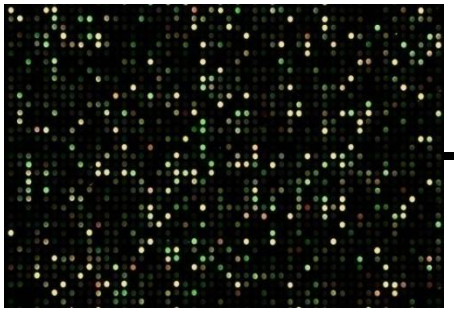


High Grade

Microarray



Low Risk



High Risk

Treatment Advice

21-Gene Recurrence Score (RS) Assay Oncotype DX (Genomic Health)

16 Cancer and 5 Reference Genes From 3 Studies

PROLIFERATION
Ki-67
STK15
Survivin
Cyclin B1
MYBL2

INVASION
Stromolysin 3
Cathepsin L2

HER2
GRB7
HER2

ESTROGEN
ER
PR
Bcl2
SCUBE2

GSTM1

CD68

BAG1

REFERENCE
Beta-actin
GAPDH GUS
RPLPO TFRC

RS Weighting:

+ 0.47 x HER2 Group

- 0.34 x ER Group

+1.04 x Proliferation Group

+ 0.10 x Invasion Group

+ 0.05 x CD68

- 0.08 x GSTM1

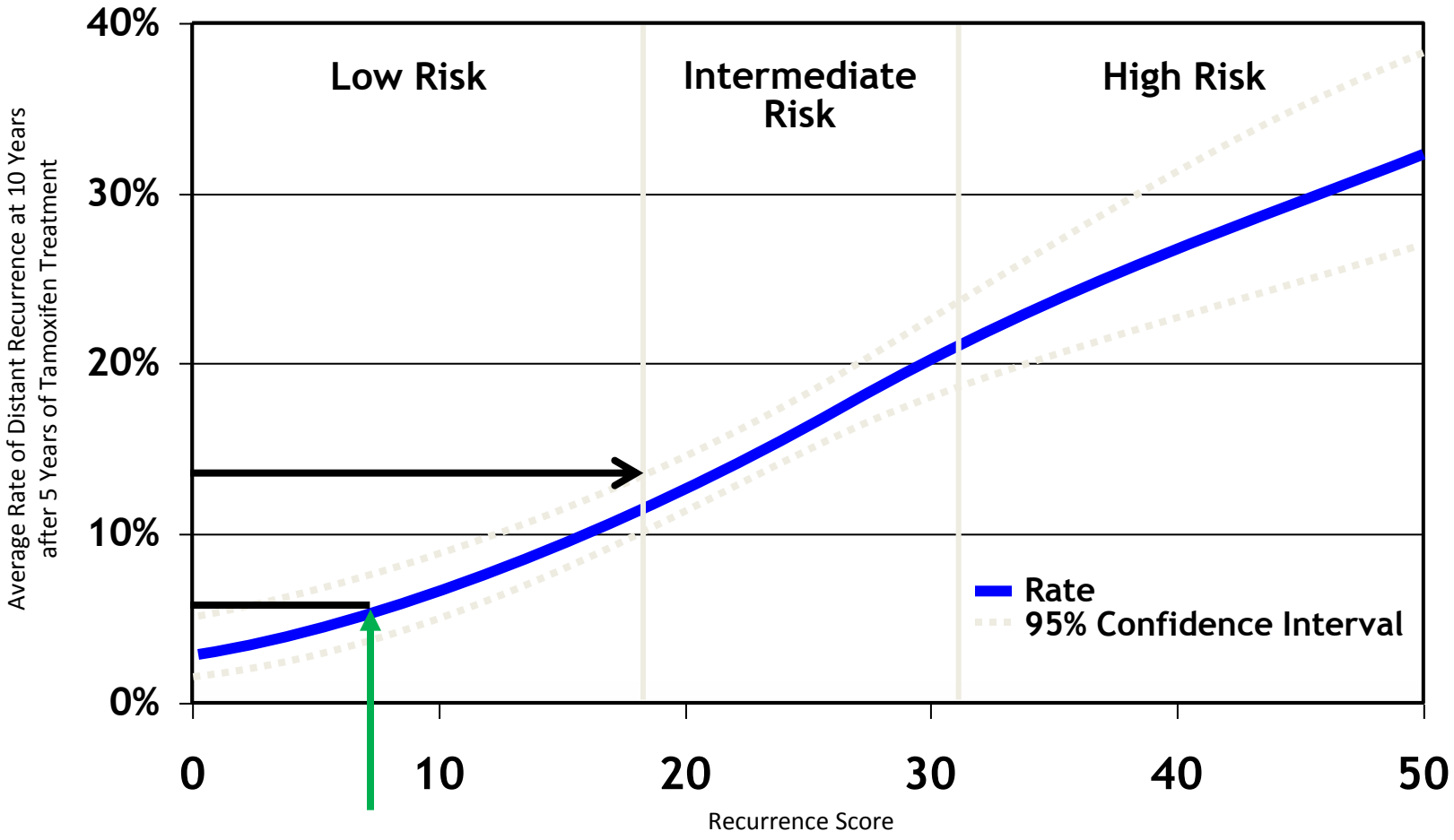
- 0.07 x BAG1

Category	RS (0 - 100)
Low risk	RS < 18
Intermediate risk	RS ≥ 18 and < 31
High risk	RS ≥ 31

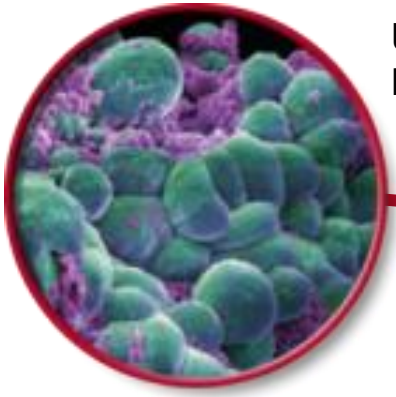
Paik et al. *N Engl J Med.* 2004;351:2817-2826.

The Recurrence Score

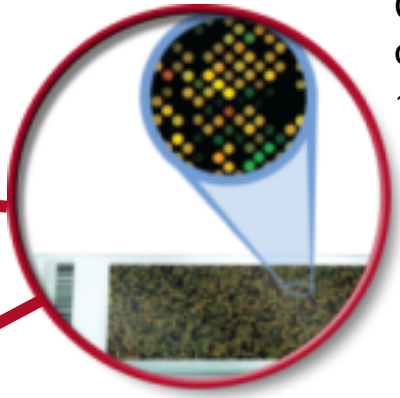
The following results are from a clinical validation study with prospectively-defined endpoints involving 668 patients. The patients enrolled in the study were female, stage I or II, node-negative, ER-positive, and treated with tamoxifen. N Engl J Med 2004; 351:2817-26.



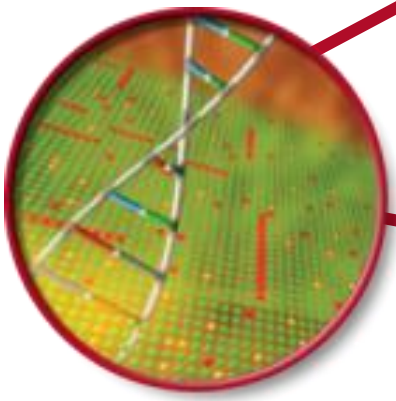
MammaPrint®: Enhanced Scientific Guidance Through Unbiased Gene Selection



Untreated Patient
Breast Tumor Samples

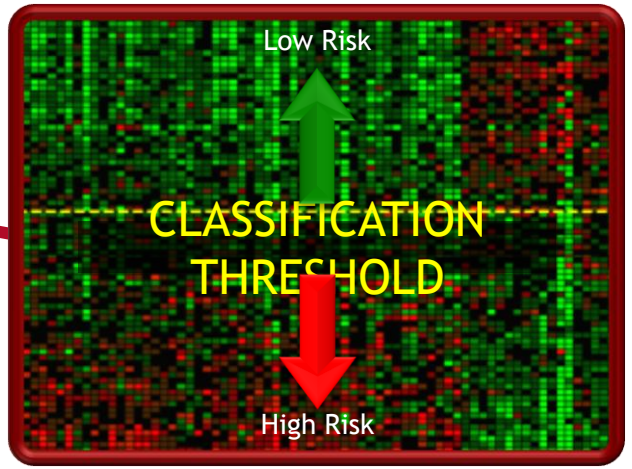


Gene Expression Analysis
of Entire Human Genome
~25,000 Genes



231 Prognostic Breast
Cancer Genes Identified

70 Most
Prognostic Genes

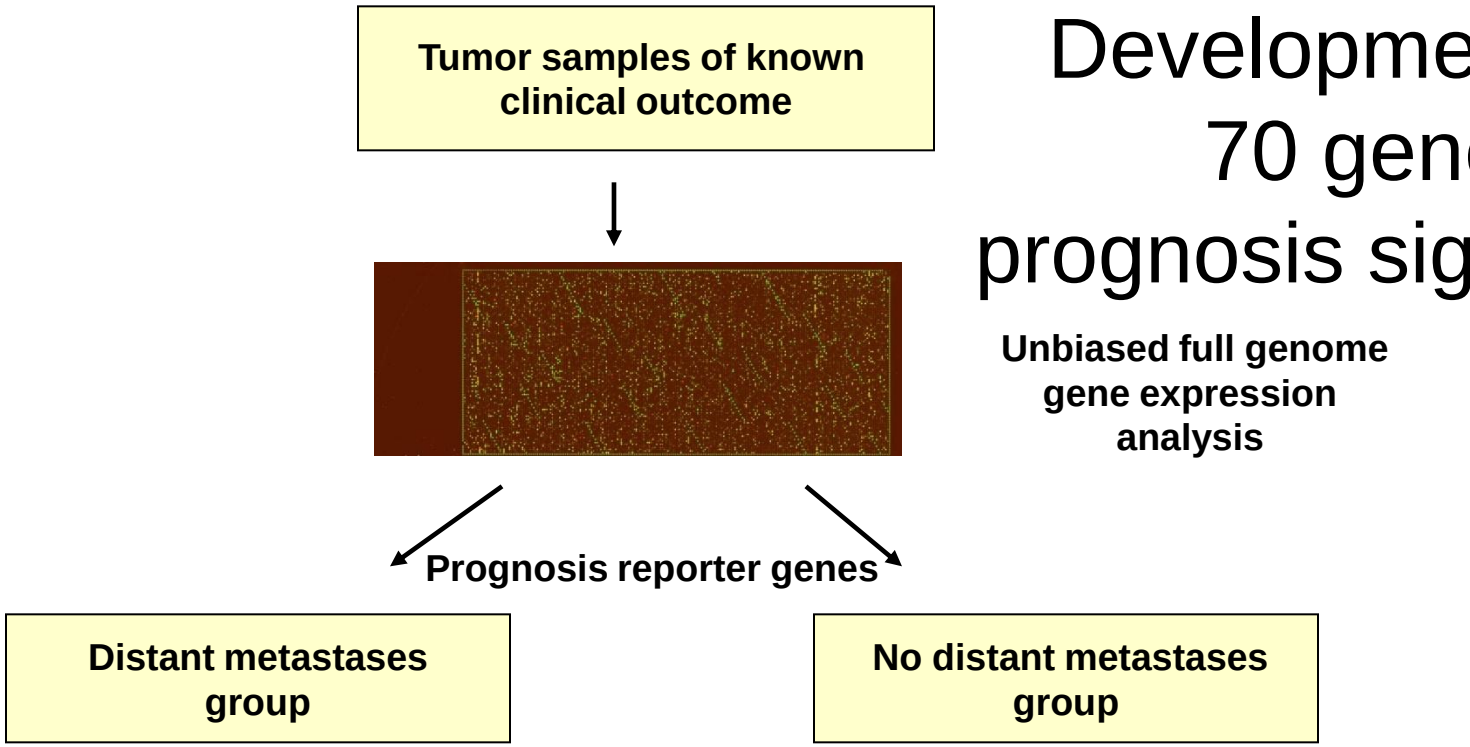


High Risk or Low Risk,
No Intermediates

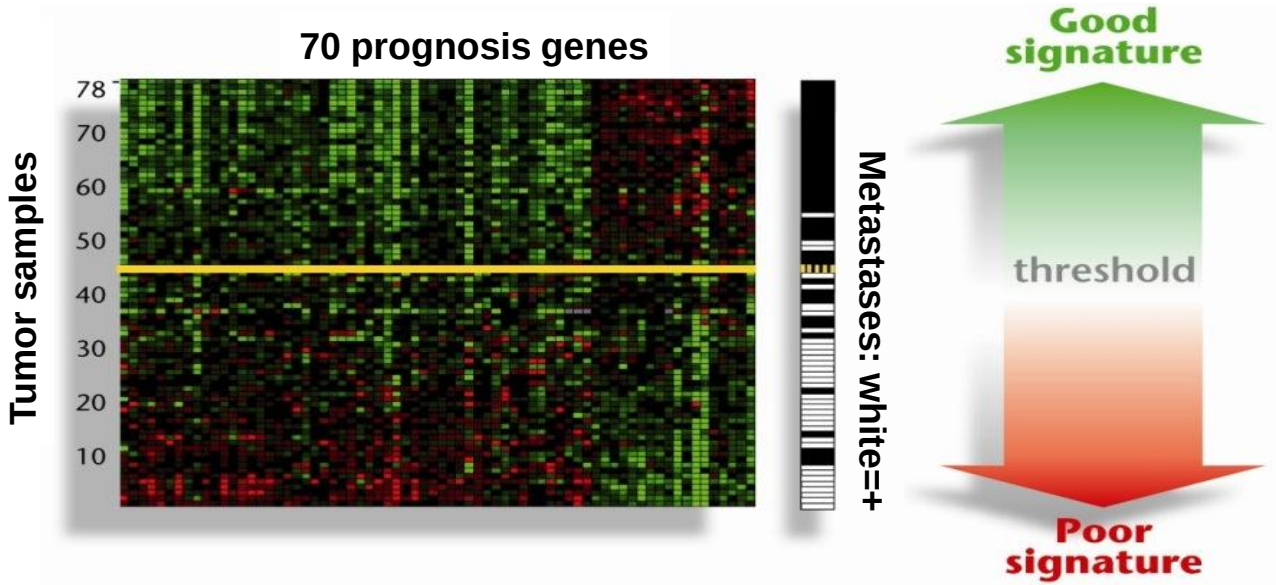
70-gene MammaPrint

- Is not just another prognostic factor
- Is designed from the beginning to tell you the metastatic potential of an individual breast cancer

Development of 70 gene prognosis signature



b



Nature, 2002

70-gene MammaPrint

- Function of majority of genes is identified and are all related to the process of dissemination

Prognostic value of the 70-gene assay

- Biologically plausible
- Better compared to conventional criteria (multivariate-analysis)
- Validated in 8 independent series

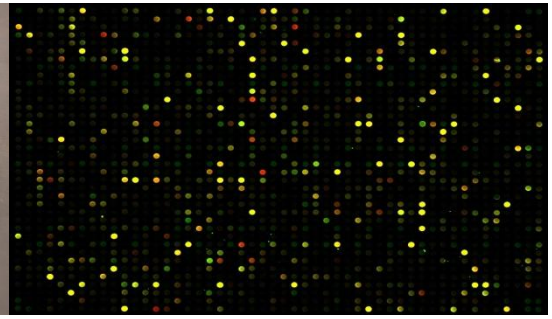
MammaPrint validation studies > 2500 patients

Validierungsstudie	Land	Reference	Jahr				
			2006	2007	2008	2009	2010
Independent European study		Buyse et al J NCI 17	**302**				
Prospective Study		de Mesquita et al. Lancet Oncology		**427**			
Dutch patient cohort		de Mesquito Breast Cancer Res Treat			**123**		
Core Needle biopsies		Mayordomo et al. ESMO Meeting			**35**		
Validation in US patients		Wittner et al. Clin Cancer Res 14			**100**		
Validation 1-3 LN+ patients		Mook et al. Breast Cancer Res Treat.			**241**		
Postmenopausal patients		Mook et al. Breast Cancer Res Treat			**148**		
Patients treated w Tamoxifen		Kok et al. (submitted)				**192**	
German patient cohort		Kunz et al. St. Gallen Conference				**140**	
Japanese patient cohort		Ishitobi et al. Jap J Clin Oncology				**118**	
Validation 4-9 LN+ patients		Saghastchian et al. St. Gallen Conf				**167**	
Neoadjuvant predictive study		Straver et al. Breast Cancer Res Treat				**162**	
Predictiveness study		Knauer et al. Breast Cancer Res Treat					**541**

MammaPrint from Research to Diagnostics

- Retrospective validation - Completed
- Prospective Technology assessment - Utility & Cost-effectiveness

- Diagnostic test - International CE marked
- Laboratory - CLIA registered
- Diagnostic test - ISO17025 certified
- Diagnostic test - CAP accredited
- Diagnostic test and clinical use - FDA approved, IVDMIA feb07
- Treatment Recommendations - Dutch Guidelines 08
- Treatment Recommendations - StGallen International Guidelines 09



Reproducibility
Test Result >98%
Success rate >95%

Glas et al,
BMC Genomics 200

Validation 1: N = 151

vd Vijver et al, N Engl J Med 347: 1999-2009, 2002

TABLE 4. MULTIVARIABLE PROPORTIONAL-HAZARDS ANALYSIS OF THE RISK OF DISTANT METASTASES AS A FIRST EVENT.

VARIABLE	HAZARD RATIO (95% CI)*	P VALUE
Poor-prognosis signature (vs. good-prognosis signature)	4.6 (2.3–9.2)	<0.001
Age (per 10-yr increment)	0.73 (0.50–1.06)	0.10
Lymph-node status (per positive node)	1.13 (1.03–1.24)	0.01
Diameter of tumor (per cm)	1.56 (1.22–2.0)	<0.001
Tumor grade		0.54
Grade 2 (vs. grade 1)	1.35 (0.61–3.0)	
Grade 3 (vs. grade 1)	1.03 (0.44–2.4)	
Vascular invasion		0.05
1–3 Vessels (vs. 0 vessels)	0.66 (0.30–1.44)	
>3 Vessels (vs. 0 vessels)	1.65 (0.98–2.8)	
Estrogen-receptor expression (per point)†	0.86 (0.56–1.31)	0.48
Mastectomy (vs. breast-conserving therapy)	1.27 (0.79–2.0)	0.32
Chemotherapy (vs. no chemotherapy)	0.37 (0.20–0.66)	<0.001
Hormonal treatment (vs. no hormonal treatment)	0.62 (0.29–1.34)	0.23

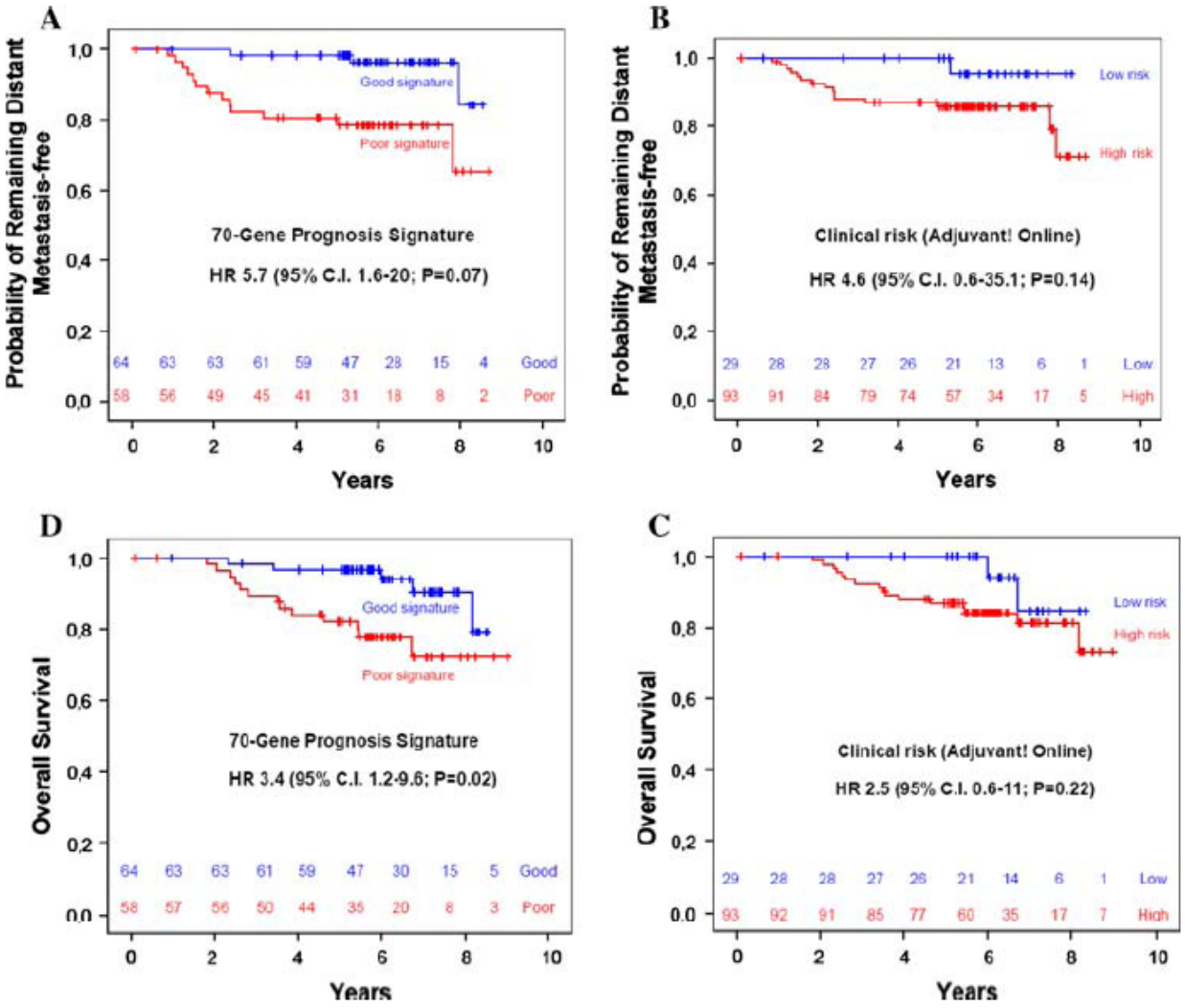
Validation 2: N = 307

Buyse M, et al.: J Natl Cancer Inst 98: 1183-92, 2006

Risk factor or classification	Time to distant metastases
Age (≤50y versus >50y)	0.86 (0.54 to 1.37) *P* = .52
Tumor size (T2 versus T1)	1.42 (0.90 to 2.23) *P* = .14
Tumor grade (good versus intermediate versus poor differentiation)	0.76 (0.54 to 1.07) *P* = .12
Estrogen receptor status (negative versus positive)	2.18 (1.37 to 3.48) *P* = .001
Adjuvant! software (high risk versus low risk)	1.68 (0.92 to 3.07) *P* = .092
Nottingham Prognostic Index (high risk versus low risk)‡	1.65 (1.02 to 2.66) *P* = .043
St Gallen criteria (high risk versus low risk)§	2.22 (0.70 to 7.08) *P* = .18
Gene signature (high risk versus low risk)‖	2.32 (1.35 to 4.00) *P* = .002

Validation 3: N = 123

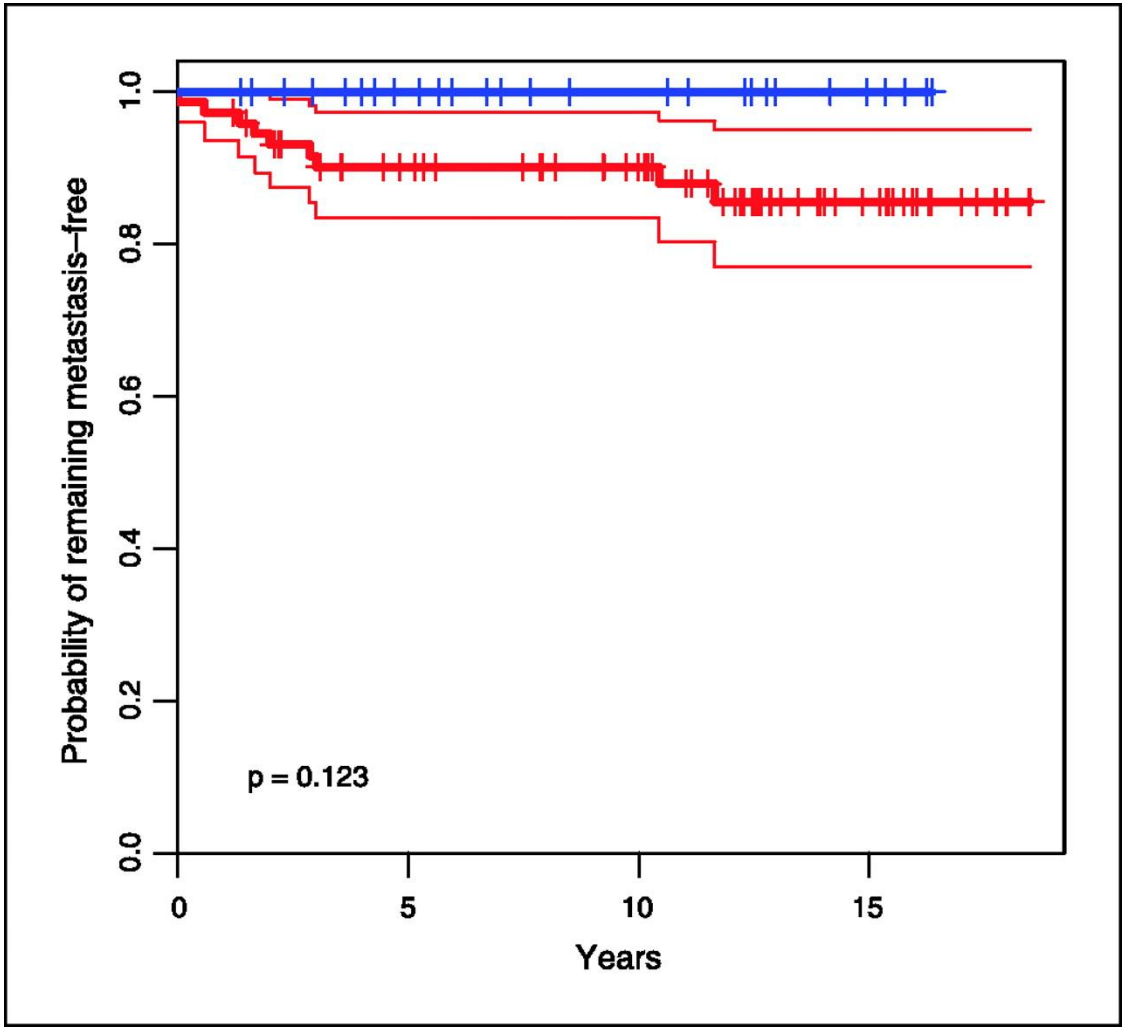
Bueno-de-Mesquita JM: Breast Cancer Res Treatm 2008



The 70-gene Signature Outperforms:
-Adjuvant Online
-St Gallen criteria
-Nottingham PI
-CBO guidelines

Validation 4: N = 100

Wittner et al., Clin Cancer Res 14: 2988, 2008



MGH series, Boston;

Time to metastasis

St.Gallen RISK Categories

1696 patients analyzed from pooled database

	All endocrine responsive patients	Highly/incompletely responsive	All patients
Low risk	**145**	**141**	**145**
Intermediate risk	**1020**	**773**	**1287**
High risk	**91**	**85**	**190**
Total	**1256/1696 = 74%**	**999/1696 = 59%**	**1622/1696 = 96%**

Median follow-up 7.08 years ± 5.02 (0.01 – 25.22)

Knauer et al, abstracts StGallen, ASCO and submitted 2009

Added value to assess risk in intermediate category by MammaPrint

Are they all at ‘intermediate’ risk?

A large meta analysis

Pooled analysis MammaPrint

1696 patients with MammaPrint

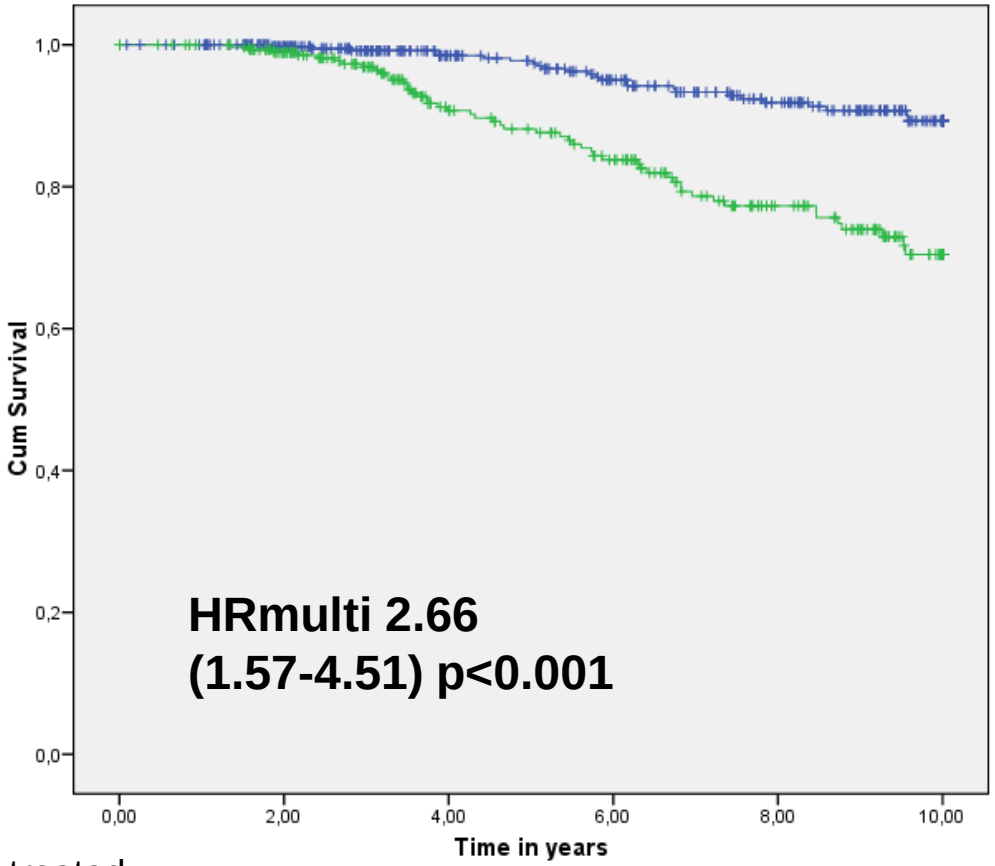
7 studies:		
295 ptn van de Vijver et al	**(<53, LN0/LN+)**	**(NEJM, 2002)**
302 ptn Buyse et al.	**(Transbig Int, <60, LN0)**	**(JNCI, 2006)**
427 ptn Bueno et al.	**(RASTER prosp, <60, LN0)**	**(Lancet Oncol, 2007)**
123 ptn Bueno et al.	**(Recent, LNneg)**	**(Br Can Res Tr, 2008)**
241 ptn Mook et al.	**(1-3 LNpos)**	**(Br Can Res Tr, 2008)**
148 ptn Mook et al.	**(age 55-70)**	**(SABCS 2007, #1063)**
160 ptn Kok et al.	**(adj tamoxifen)**	**(unpublished)**

Median follow-up 7.08 years (0.01 – 25.22)

Knauer et al, abstracts StGallen, ASCO and submitted 2009

Intermediate Risk by MammaPrint

Breast Cancer Specific Survival
for highly and incomplete endocrine responsive HER2 neg patients
n = 714



good signature
n = 422 (59%)

poor signature
n = 292 (41%)

Note: untreated and treated
Knauer et al, abstracts StGallen, ASCO and submitted 2009

Issues in early breast cancer

- Is good pathology as good?
- Small cancers good prognosis?
- Her 2 overexpression: chemo?
- MammaPrint and chemo-effect

Issues in early breast cancer

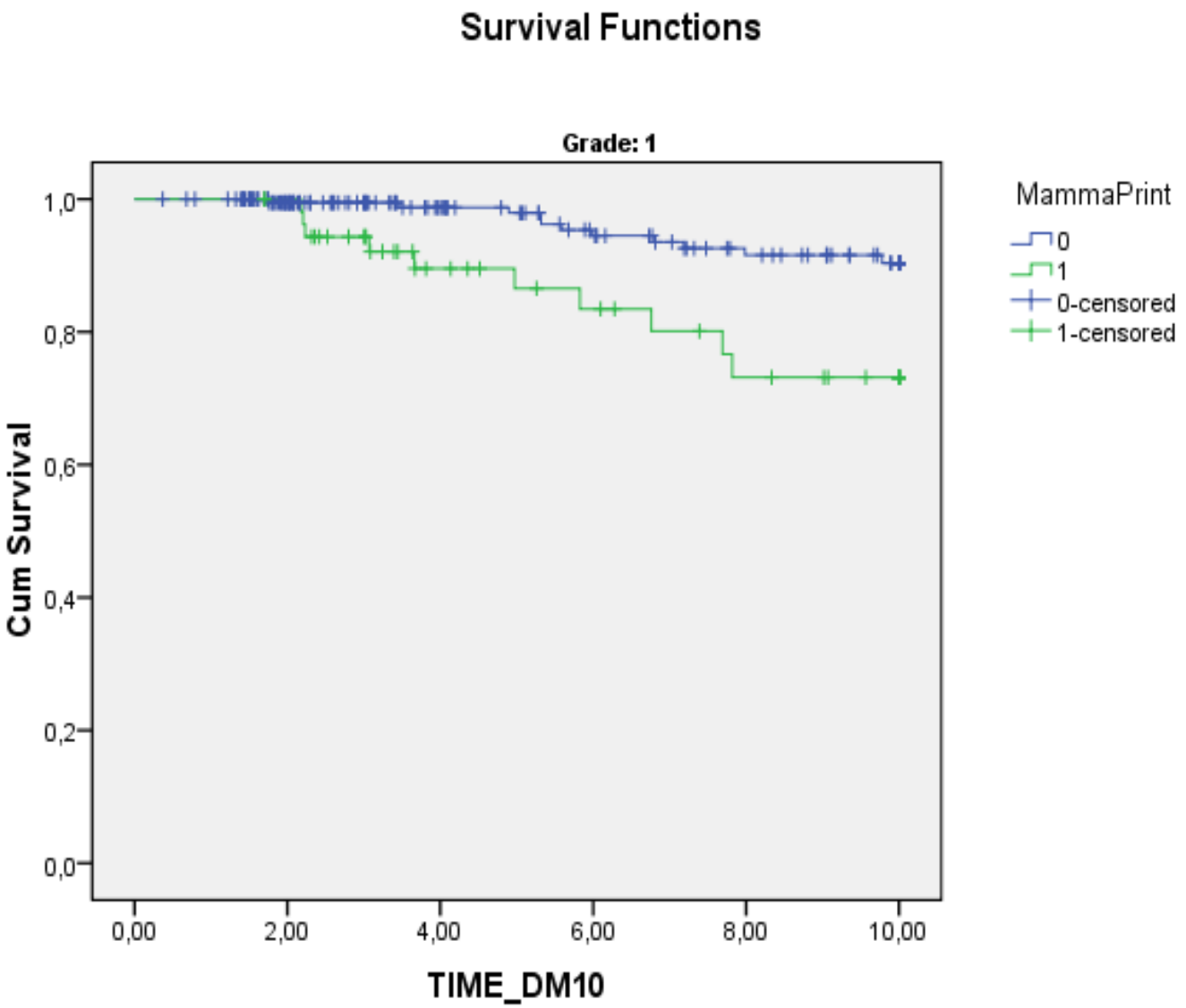
- Is good pathology as good?

Is Grading the golden standard….

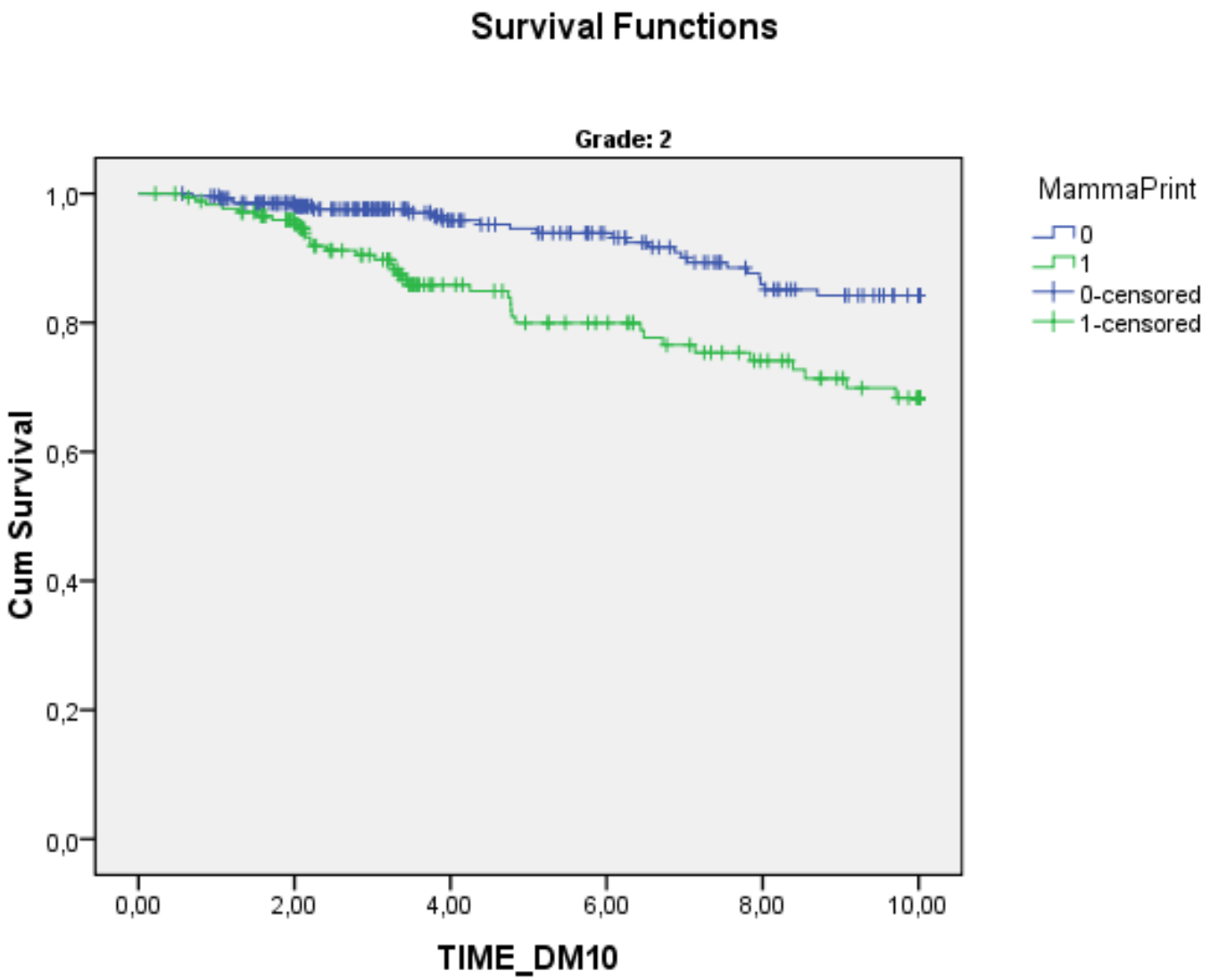
- Or can we do better?

Patients (n=965)	Characteristic	n (%)
Age	≤ 50 years > 50 years	509 (53%) 456 (47%)
Tumor size	T1a/b T1c	140 (14%) 825 (86%)
Lymph node status	Node negative Node positive n.a.	716 (74%) 241 (25%) 8 (1%)
Histological grade	Grade 1 Grade 2 Grade 3 n.a.	280 (29%) 412 (43%) 262 (27%) 11 (1%)
Estrogen receptor status	Positive (≥10%)	808 (84%)
Progesterone receptor status	Positive (≥10%)	554 (57%)
Her2-status	Positive	91 (9%)
Adjuvant treatment	No adjuvant therapy Endocrine therapy Chemotherapy Both	562 (59%) 182 (19%) 100 (10%) 117 (12%)

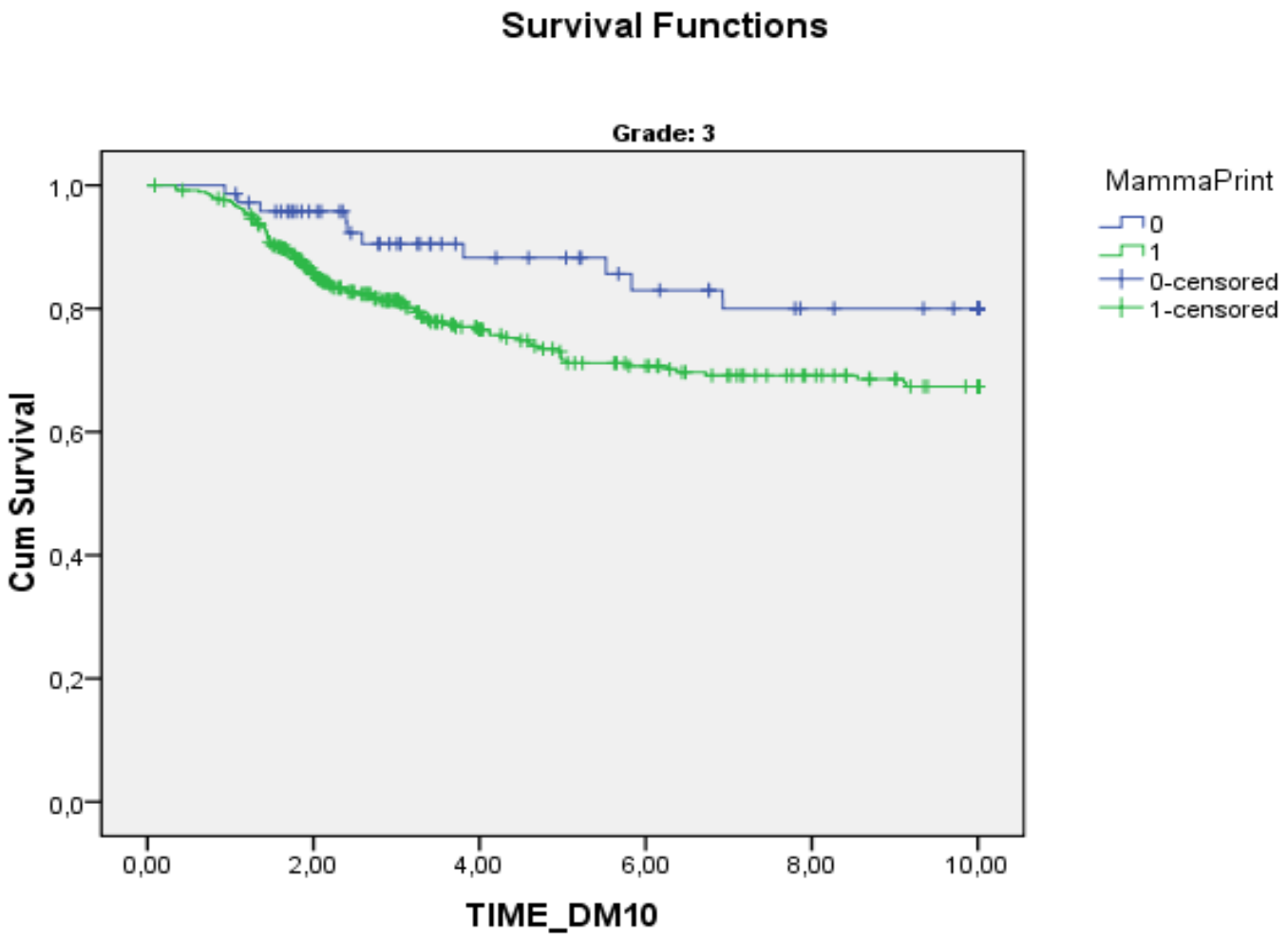
DDFS N0


Survival Functions
Grade: 1
Cum Survival
1,0
0,8
0,6
0,4
0,2
0,0
0,00
2,00
4,00
6,00
8,00
10,00
TIME_DM10
MammaPrint
0
1
0-censored
1-censored

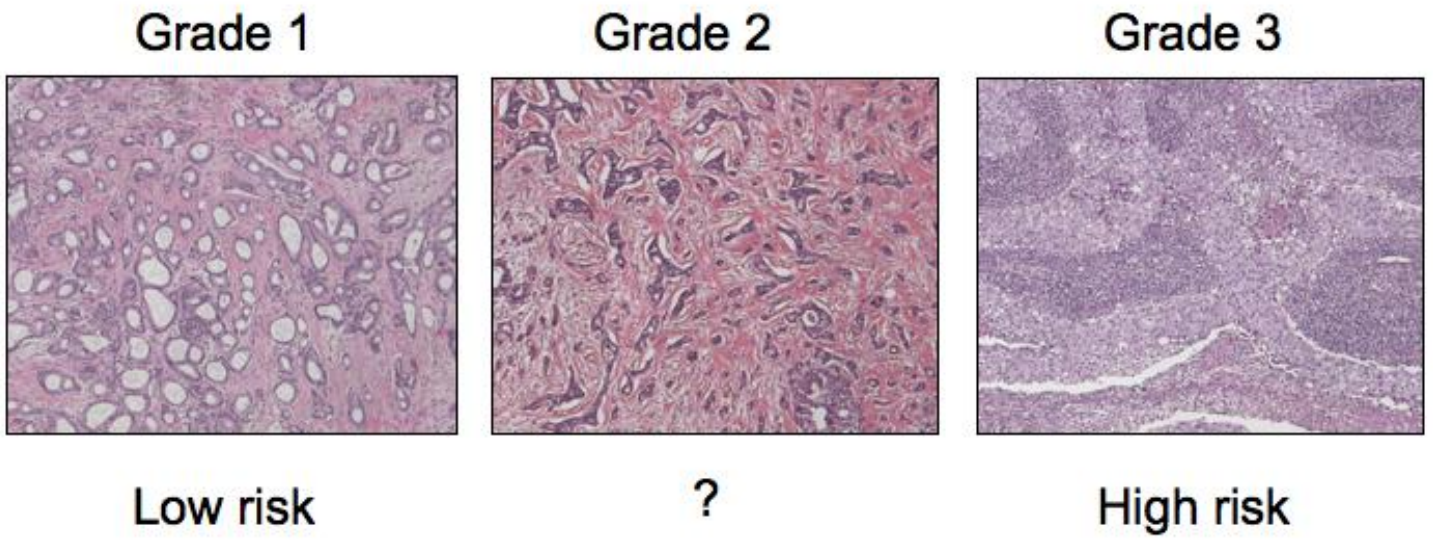
DDFS N0


Survival Functions
Grade: 2
Cum Survival
1,0
0,8
0,6
0,4
0,2
0,0
0,00
2,00
4,00
6,00
8,00
10,00
TIME_DM10
MammaPrint
0
1
0-censored
1-censored

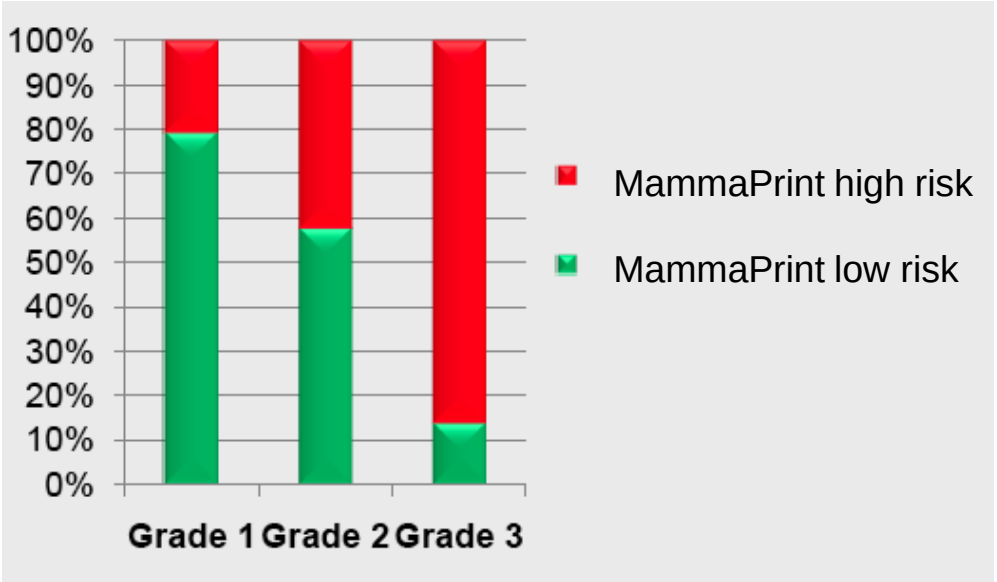
DDFS N0


Survival Functions
Grade: 3
Cum Survival
1,0
0,8
0,6
0,4
0,2
0,0
0,00
2,00
4,00
6,00
8,00
10,00
TIME_DM10
MammaPrint
0
1
0-censored
1-censored

MammaPrint adds to grading of breast cancer



764 of 1630 patients (47%) were classified as good prognosis and 866 (53%) as poor prognosis by MammaPrint
Histological grading was centrally reviewed for all patients



Issues in early breast cancer

- Small cancers good prognosis?

Patient inclusion criteria:

T1 breast cancer

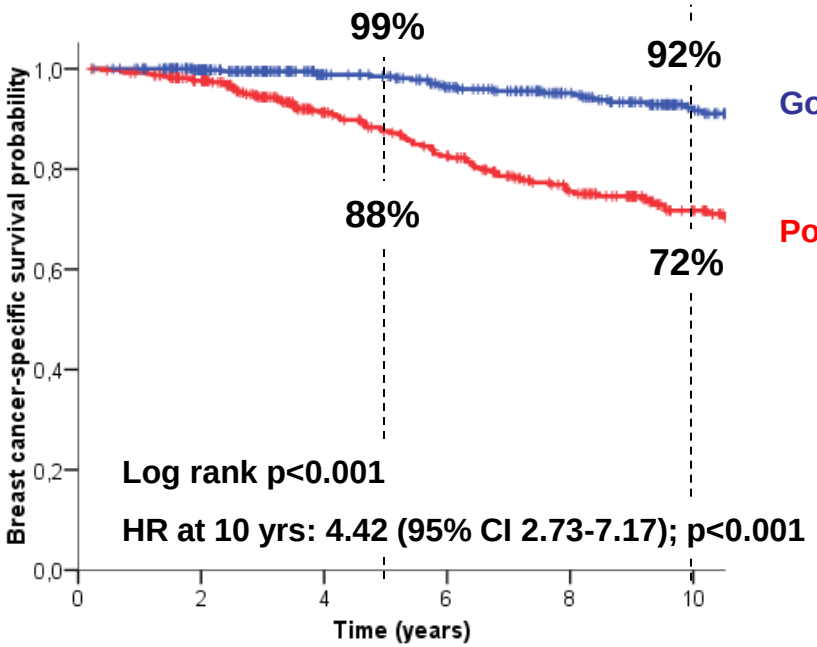
Irrespective of
- Age
- Nodal status
- ER, PR, Her2-status

=> 965 patients

Median follow-up 7.1 years (0.2-25.2)

MammaPrint and Tumorsize T1c BCSS

11 – 22 mm Tumors



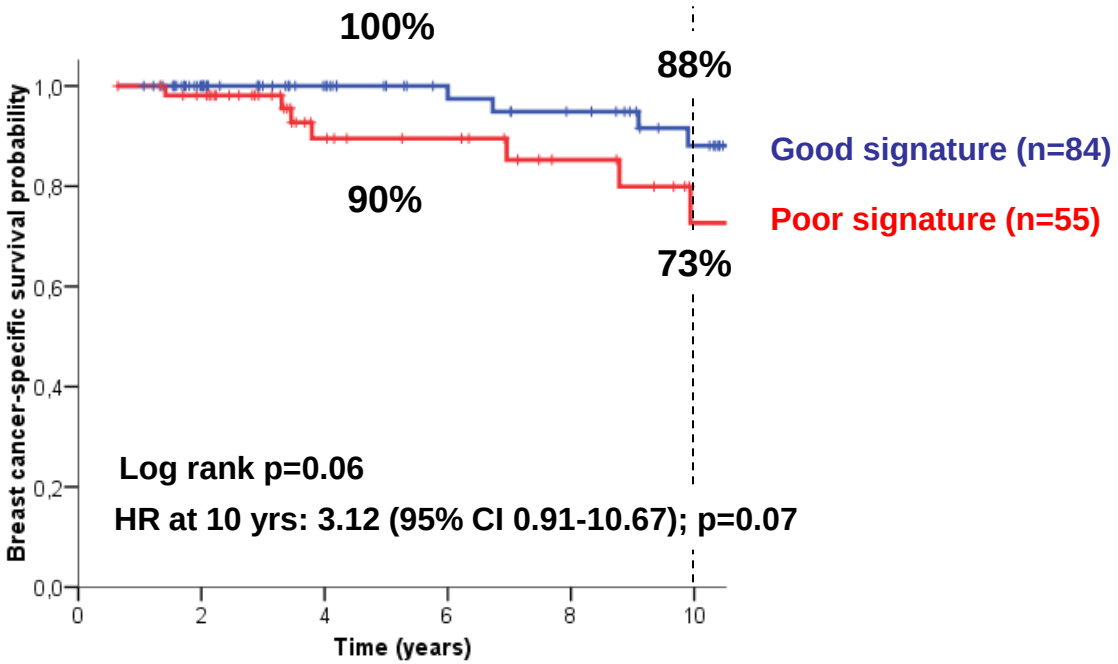
Good	441	392	294	261	218	154
Poor	384	350	256	215	166	114

T1c tumors derived from pooled database of all MammaPrint validation studies (all, n=1696)

Mook et al, Ann Surg Oncol, 2010

MammaPrint and Tumorsize T1ab BCSS

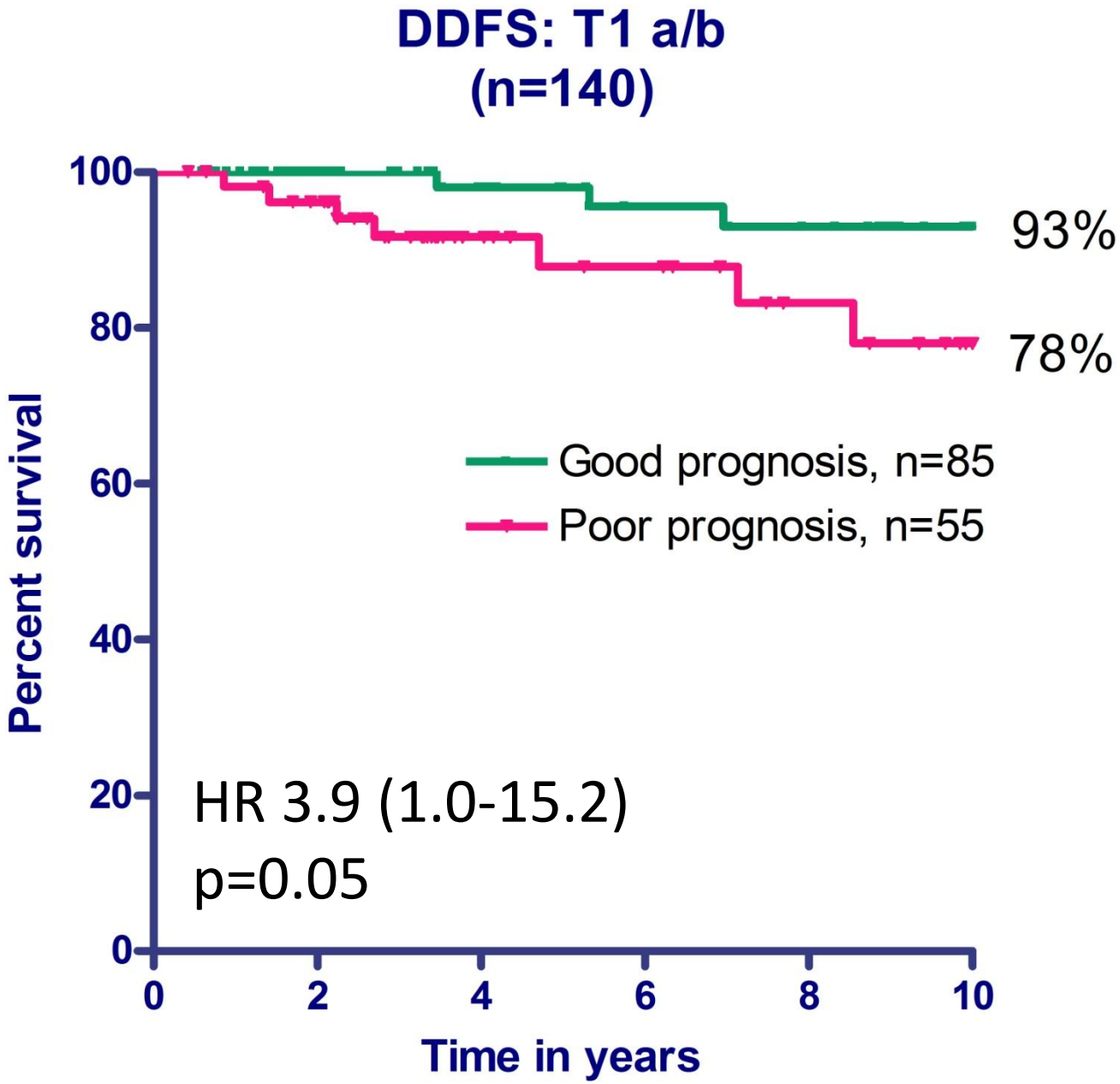
0 – 10 mm Tumors



Good	84	69	50	39	34	25
Poor	55	51	28	24	17	10

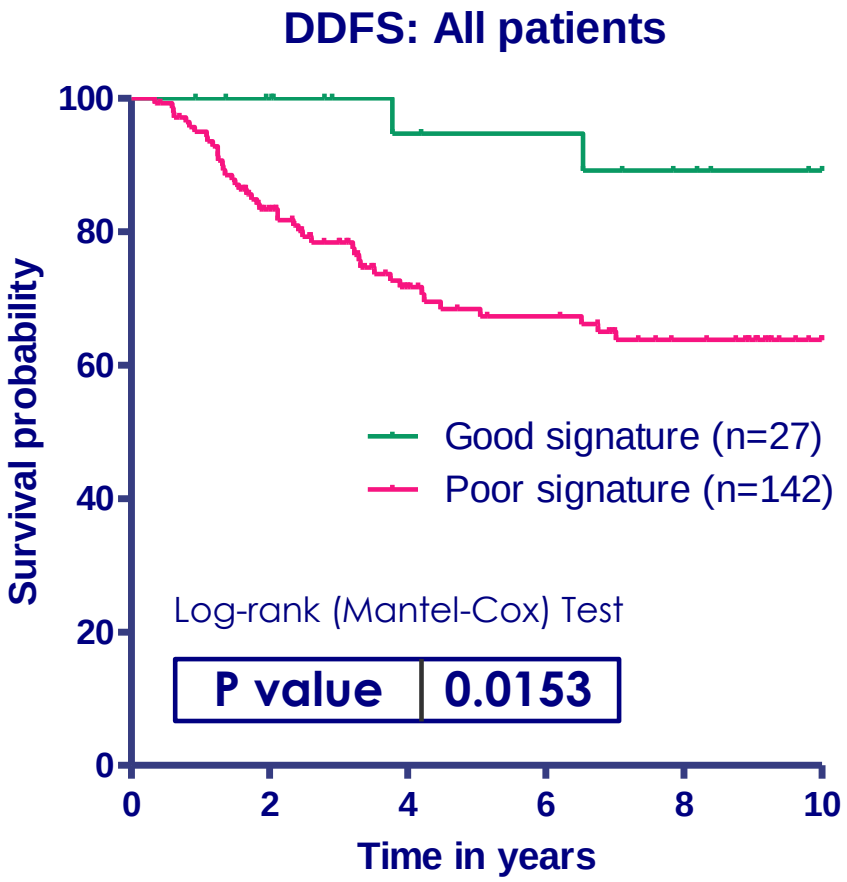
T1ab tumors derived from pooled database of all MammaPrint validation studies (all, n=1696)

Mook et al, Ann Surg Oncol 2010


DDFS: T1 a/b
(n=140)
100
80
60
40
20
0
Percent survival
93%
78%
Good prognosis, n=85
Poor prognosis, n=55
HR 3.9 (1.0-15.2)
p=0.05
0
2
4
6
8
10
Time in years

And Her-2 positive BC….

- Always poor prognosis?



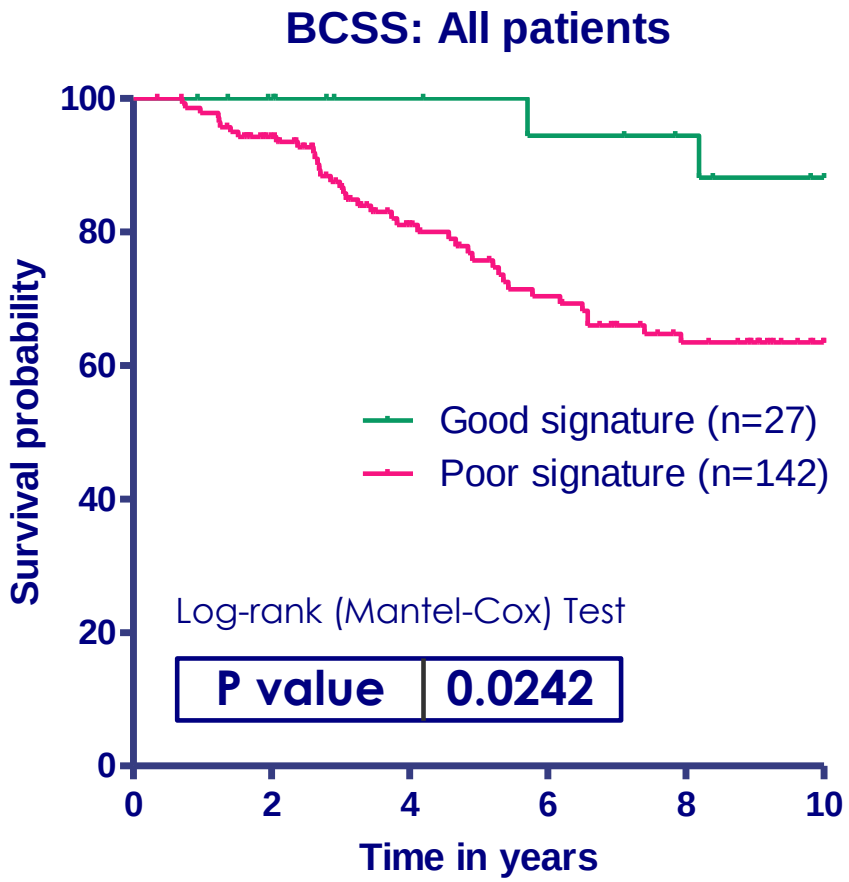
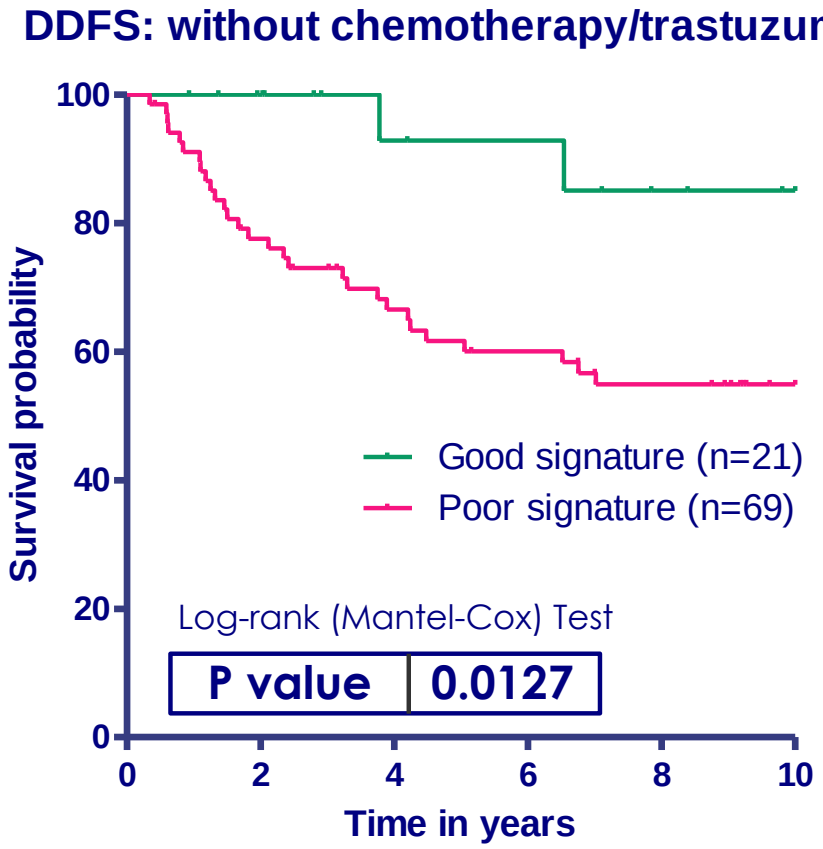


Figure 1:
Distant disease-free survival (LEFT) and breast cancer-specific survival (RIGHT) according to the 70-gene signature for all 169 Her2-positive breast cancer patients.

Michael Knauer et al.



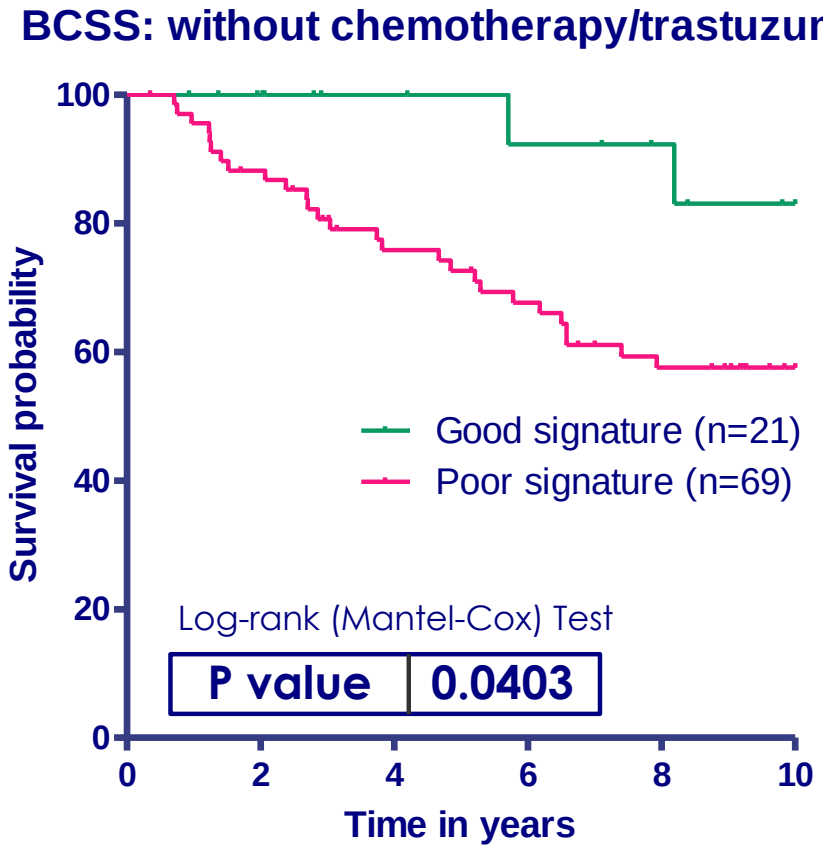
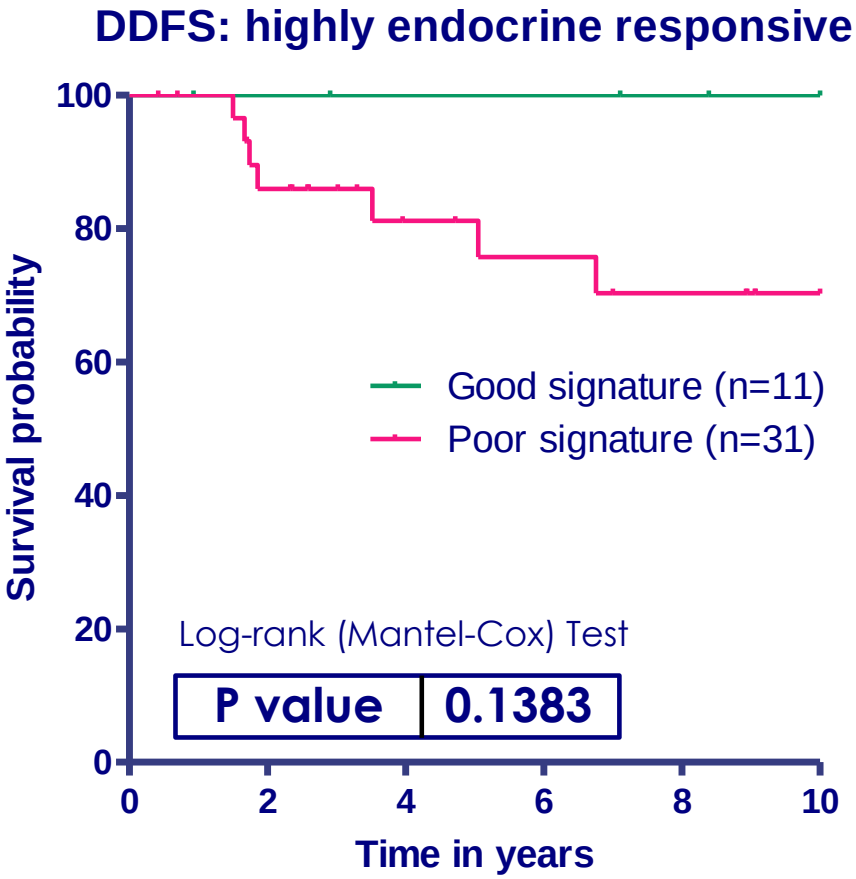


Figure 2:
Distant disease-free survival (LEFT) and breast cancer-specific survival (RIGHT) according to the
70-gene signature for 90 patients without adjuvant chemotherapy or trastuzumab.

Michael Knauer et al.



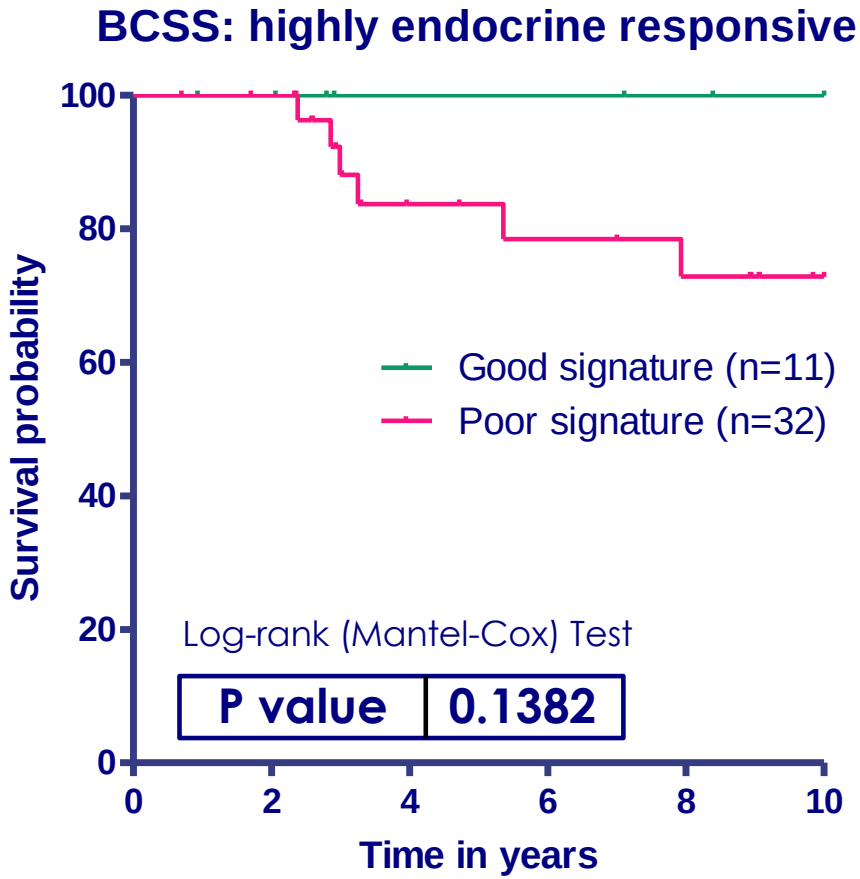


Figure 3:
Distant disease-free survival (LEFT) and breast cancer-specific survival (RIGHT) according to the
70-gene signature for 42 patients with highly endocrine-responsive tumors according to the St.Gallen criteria. Out of 11 low risk patients, 7 were untreated, 4 received chemotherapy and one of those received trastuzumab.

Michael Knauer et al.

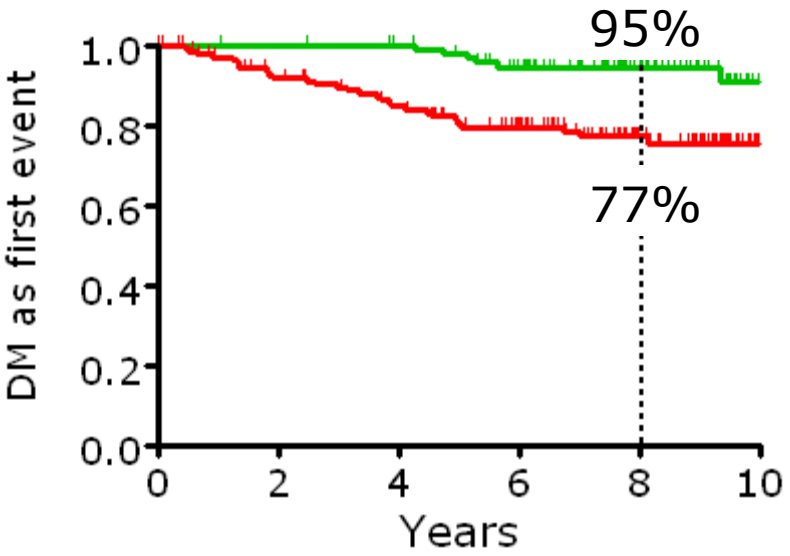
And Node +ve Breast Cancer?

- Always indication for chemotherapy?

70-gene Profile and Prognosis in Breast Cancer with 1-3 Axillary Lymph Node Metasases
S. Mook et al., Breast Cancer Res Treatm 2008.

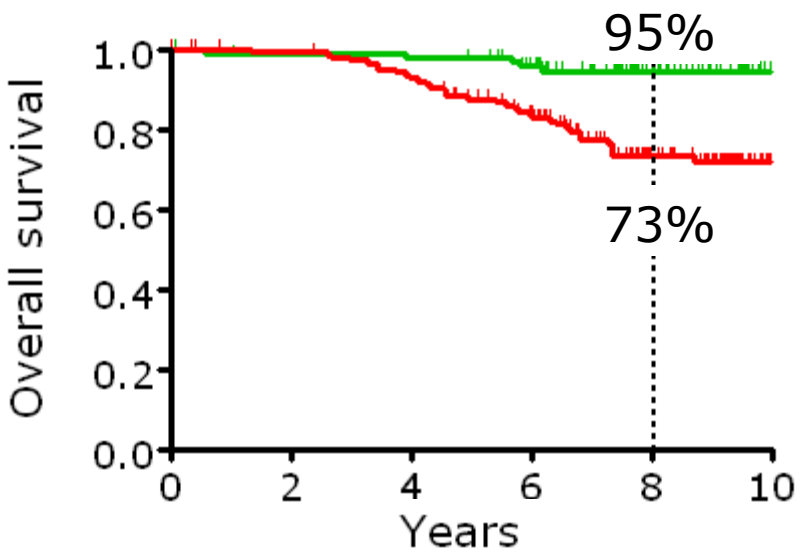
Good profile (n=99)
Poor profile (n=142)

Distant metastases as first event



HR 4.1
(95%CI 1.7 – 10.0), p=0.002

Overall survival



HR 5.4
(95%CI 2.1 – 13.8), p<0.001

Good profile: sufficiently low risk?

1-3 positive nodes, all patients (n=241)	8-yr OS	SE
Good profile (n=99)	**95%**	2
Poor profile (n=142)	73%	4

Chemotherapy (n=128)	8-yr OS	SE
Good profile (n=39)	**95%**	4
Poor profile (n=89)	69%	6

No chemotherapy (n=101)	8-yr OS	SE
Good profile (n=57)	**94%**	3
Poor profile (n=44)	77%	7

Adjuvant Chemotherapy and 70 gene prognosis signature Clinical Utility and Clinical Benefit

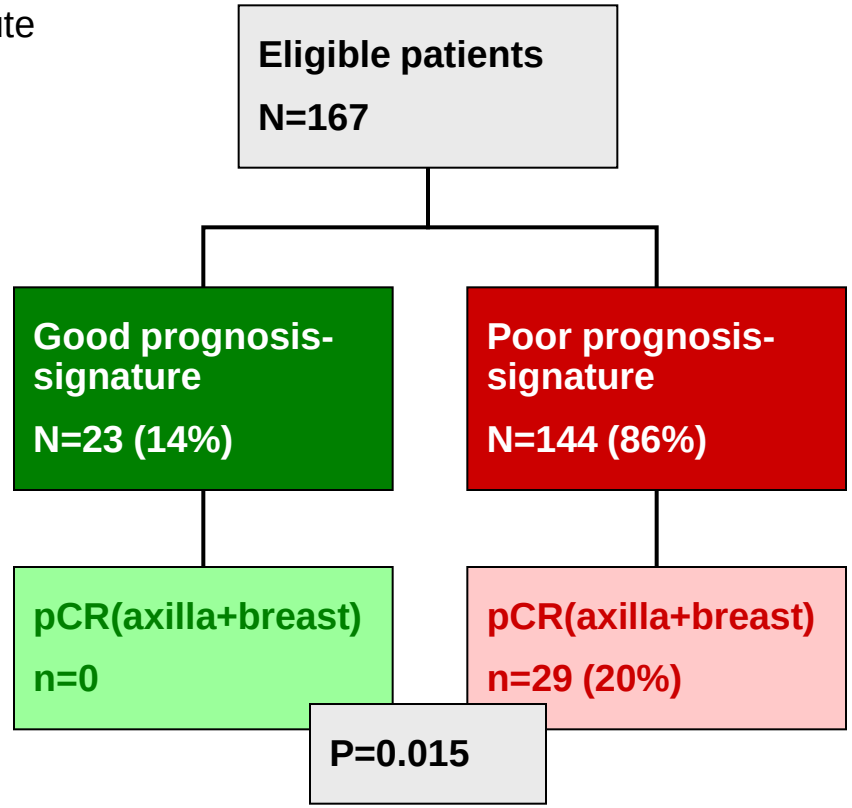
- 70 gene Low Risk Signature group has low risk for recurrence, and does not show significant chemo benefit
- 70 gene High Risk signature patients show significant neo-adjuvant chemo-sensitivity
- 70 gene High Risk Signature Patients show substantial Clinical Benefit of Adjuvant Chemotherapy (Cave: not a randomized trial)

Issues in early breast cancer

- MammaPrint and chemo-effect

Benefit of neo-adjuvant chemotherapy for MammaPrint high risk patients

- Netherlands Cancer Institute
- 2 clinical trials
- T-stage >3 cm and/or LNplus (SNB/FNA)
- ultrasound guided 14 gauge biopsies
- MRI imaging
- Pathology



- Antracycline-like
- Antracyclin-Taxane
- Taxane

- pCR:
- pathological
- complete remission

MammaPrint low risk signature → no benefit of chemotherapy

MammaPrint high risk signature → benefit of chemotherapy

Straver et al, BCRT 2009

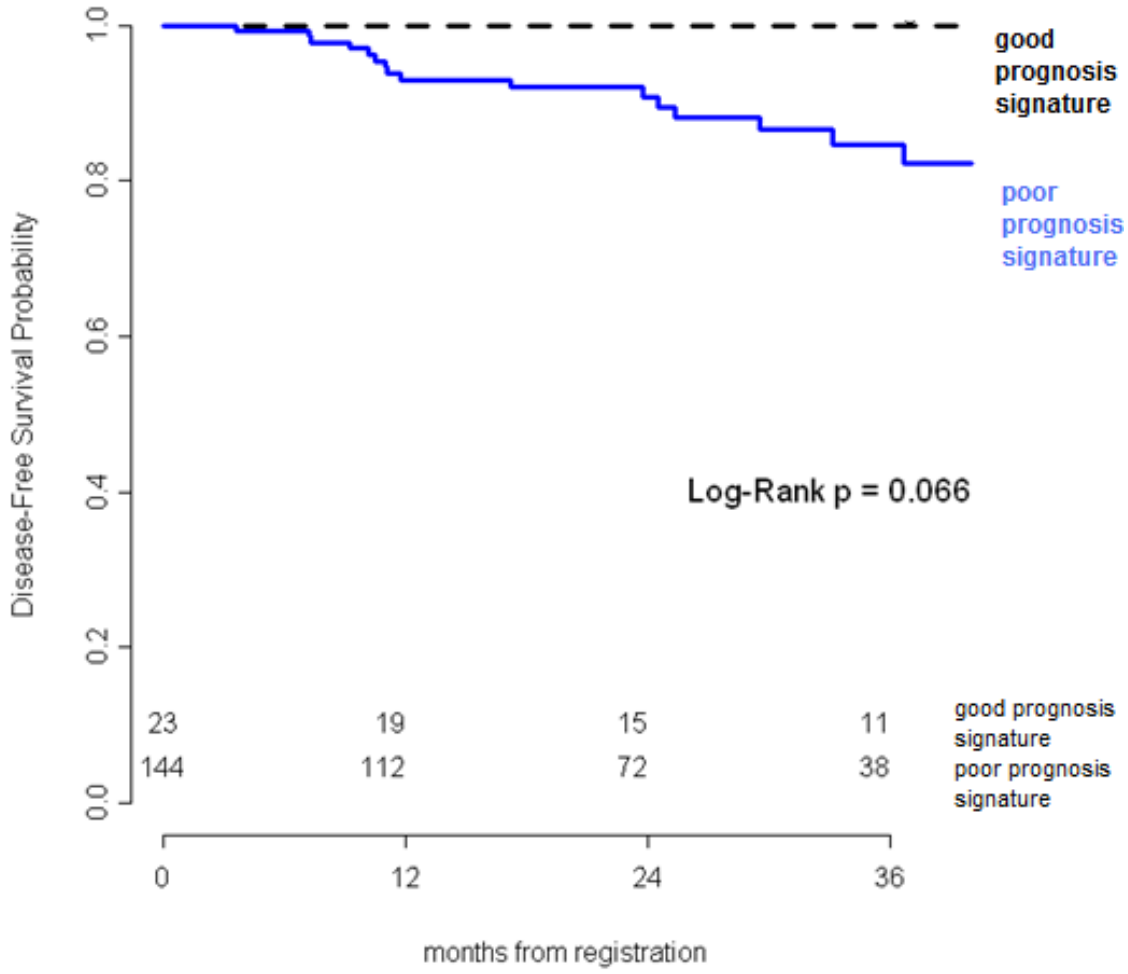
Neo-adjuvant Standard Chemotherapy and MammaPrint Clinical Benefit

- 70 gene MammaPrint High Risk Signature patients show significantly higher chemosensitivity
- All pCR are found in the High Risk Signature group

High Risk Signature Patients show Clinical Benefit of Chemotherapy

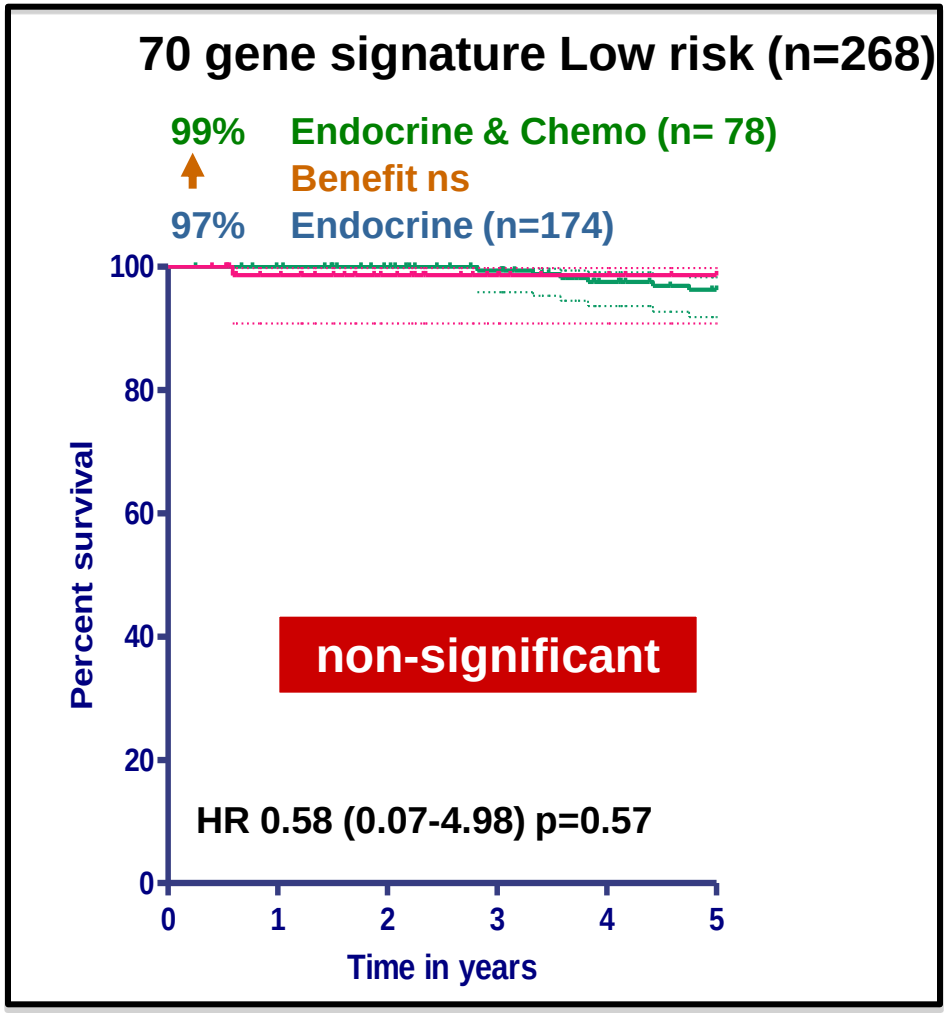
Straver et al, BCRT 2009

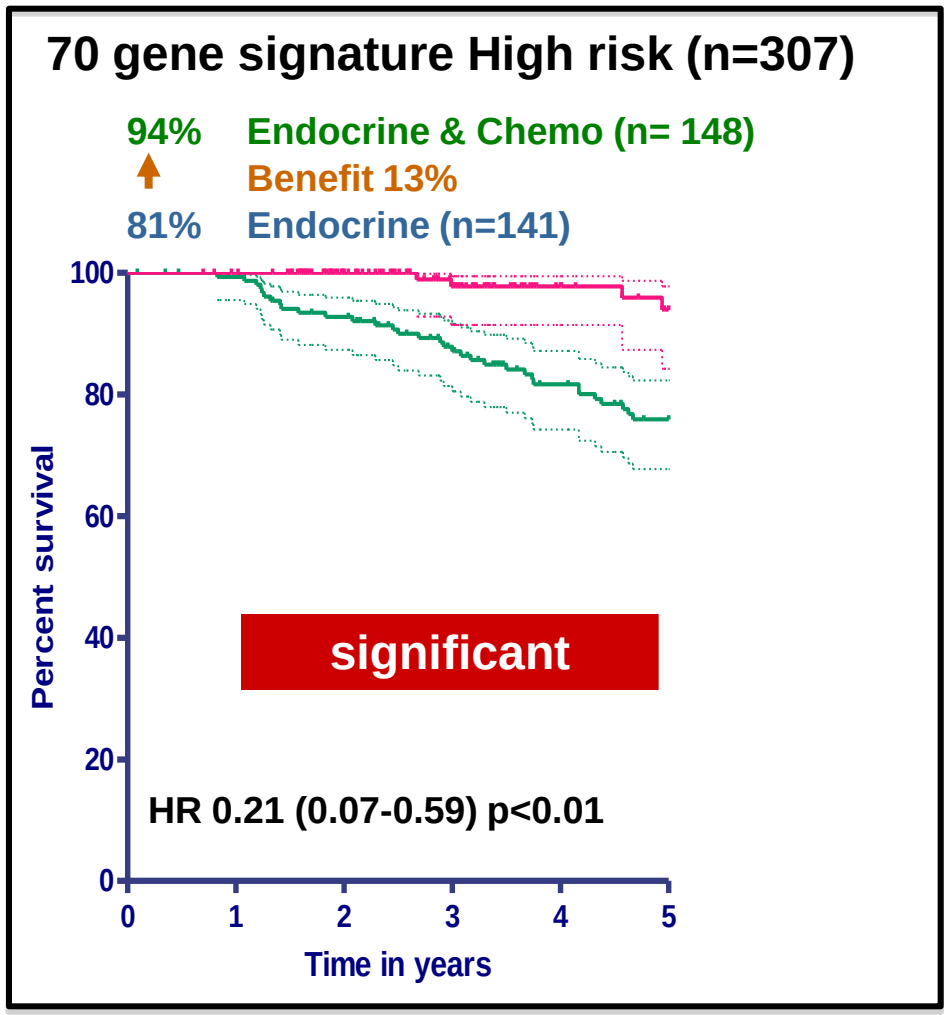
So far, no recurrences in MammaPrint good prognosis group



Straver et al 2009, Br Cancer Res and Treatment

Breast Cancer Specific Survival (5 yrs)
Endocrine vs Endocrine-Chemo
within 70 gene low and high risk signature (n=575)





Interaction term for differential effect p=0.45; *Cave*: not a randomized trial

Knauer et al, abstracts StGallen, ASCO 2009, BCRT 2010, Albain et al 2009

Cox multivariate analysis: Backward Stepwise DDFS at 10 years for ET vs. ET + CT

Variable	p-value	HR	95% CI
Age	0.307	1.02	0.99-1.05
Tumor-Diameter	0.011	1.03	1.01-1.06
LN-status	0.136	1.17	0.95-1.44
Grade	0.024	1.78	1.08-2.95
ER-status	0.670	0.86	0.43-1.72
PR-status	0.012	0.48	0.27-0.85
Her2-status	0.398	1.33	0.69-2.55
ET vs. ET + CT	0.011	0.26	0.09-0.74

Adjuvant Standard Chemotherapy and MammaPrint Clinical Benefit

- MammaPrint High Risk signature patients show significant chemo-sensitivity
- MammaPrint Low Risk Signature group does not show significant chemo benefit

High Risk Signature Patients show substantial Clinical Benefit of Adjuvant Chemotherapy

(Cave: not a randomized trial)

Moving forward
Genomics in Breast Cancer

- Science: Prospective evaluation 70 gene MammaPrint signature and therapy benefit, 6000 patients (TRANSBIG-MINDACT)
- Science: Provide comprehensive biobank and standard molecular biological assays to integrate knowledge on tumor type, germline status (TRANSBIG-MINDACT)

MINDACT trial

- Is not to validate the prognostic value of the 70-gene MammaPrint
- Will tell us if chemotherapy is rightfully witheld to patients with a MP good prognosis who would have been advised chemotherapy on the basis of current clinical criteria within strict limits: 5 yrs breast cancer specific survival of 93-95%.

EORTC 10041 BIG 3-04 trial: MINDACT
6,000 Node neg & 1-3 N+ women

PI's: Martine Piccart, Emiel Rutgers, Fatima Cardoso

Evaluate Clinical-Pathological risk and 70-gene signature risk

55%

N=3300

Clinical-pathological and 70-gene both HIGH risk

32%

Discordant cases

Clin-Path HIGH 70-gene LOW

Clin-Path LOW 70-gene HIGH

N=1920

R-T

Use Clin-Path risk to decide Chemo or not

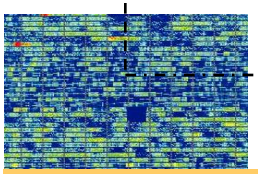
Use 70-gene risk to decide Chemo or not

13%

N=780

Clinical-pathological and 70-gene both LOW risk

Chemotherapy



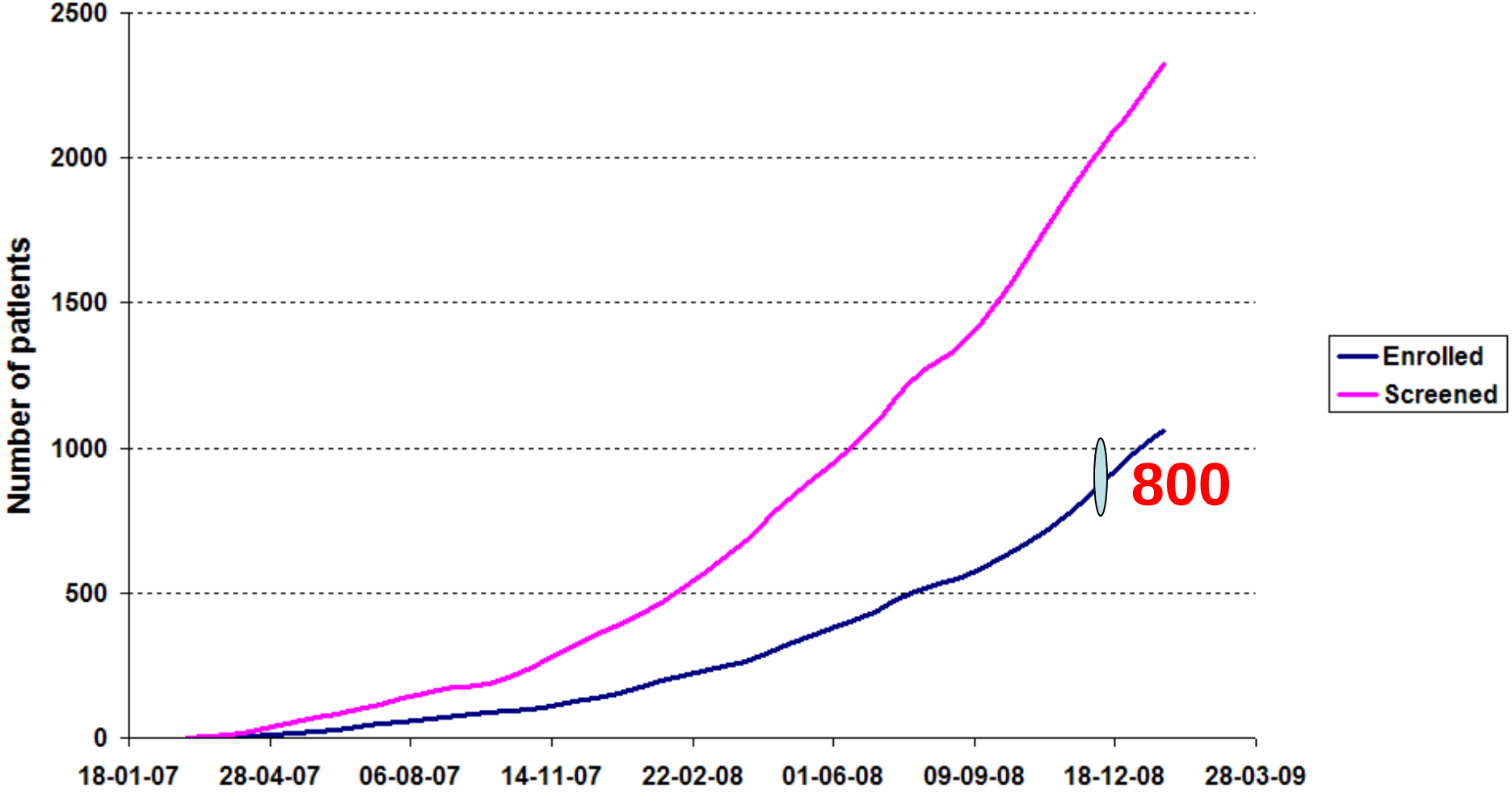
Endocrine therapy

potential chemotherapy sparing in 10-15% pts, without affecting survival

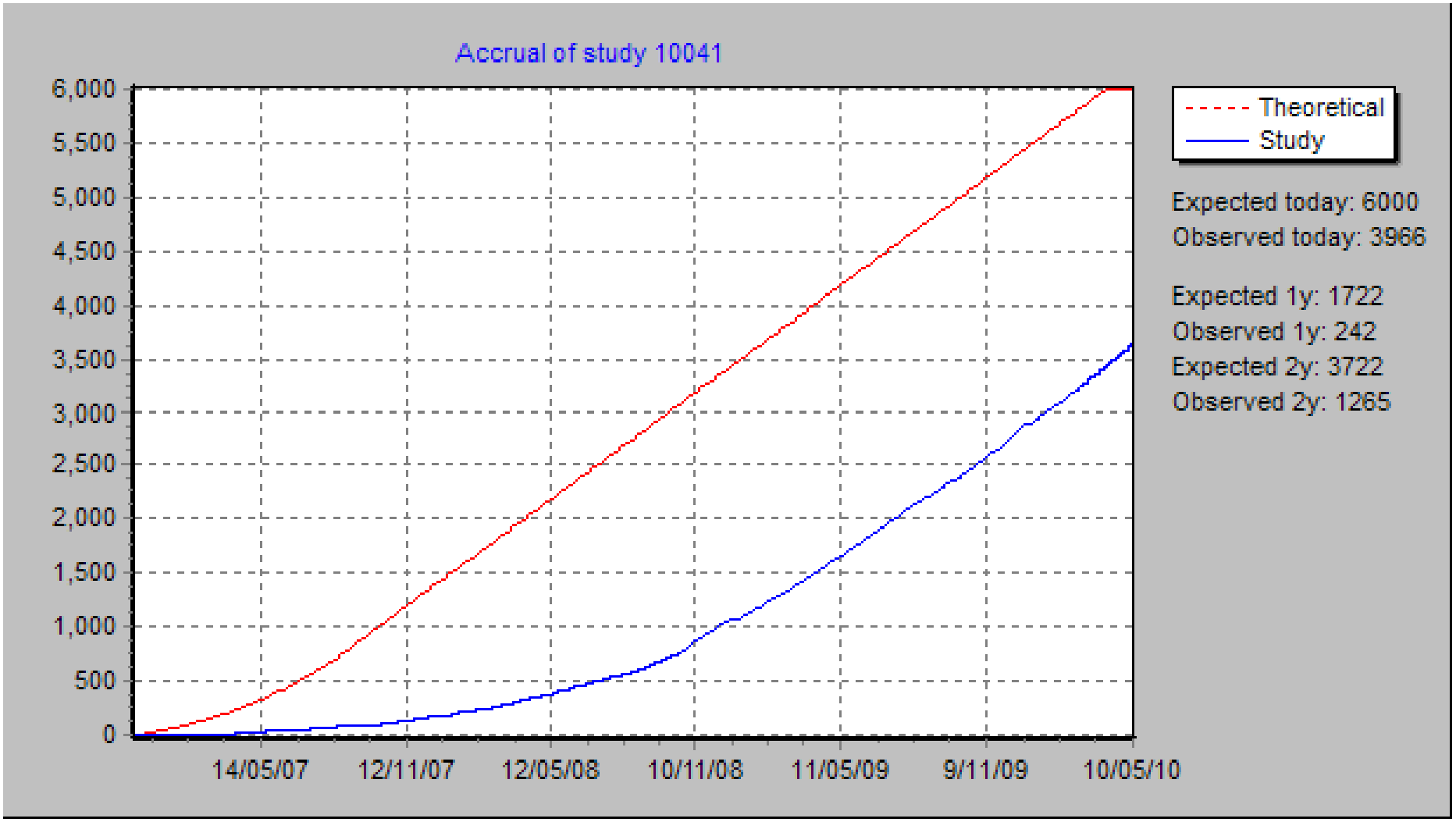
PRE-SPECIFIED PILOT PHASE FIRST 800 PTS TO ENSURE:

- **Logistically feasible**
- **Unbiased patient recruitment**
- **Less CT in genomic-based risk group than in clinical-based risk group**
- **Compliance**

MINDACT RECRUITMENT IN THE PILOT PHASE



MINDACT ENROLLED BY July 26 2010
after registration of 7183 pts.



Unbiased recruitment?

The patient population in the trial as compared to the patients from the validation series (all node -)

Older

Fewer ER-, fewer HER2+

Tumor size smaller

Tumor grade comparable

- **Expected fraction of clinical high risk patients 77% vs. observed 42.4%.**

- **Change in biology of breast cancer and/or more screening detected?**

RISK CROSS-TABLE

Clinical risk by 70 gene risk, at enrollment (overall % ages)			
	Clinical risk at enrollment		
	Low risk (N=461)	High risk (N=339)	Total (N=800)
	N (%)	N (%)	N (%)
70 gene risk at enrollment			
Low risk	386 (48.3)	141 (17.6)	527 (65.9)
High risk	75 (9.4)	198 (24.8)	273 (34.1)

Discordant cases: 27%

Estimates:
pC = 339/800 (42%)
pG = 273/800 (34%)
pC – pG = 8.25%, 95% CI = 4.69% - 11.81% (p < 0.0001)

WAS CHEMO ACTUALLY GIVEN? COMPLIANCE!

Chemotherapy administration (best current knowledge) by assignment to chemotherapy			
	Treatment decision outcome		
	chemo (N=309) N (%)	no chemo**** (N=491) N (%)	Total (N=800) N (%)
Chemo received			
No	21* (6.8)	472 (96.1)	493 (61.6)
Yes	268 (86.7)	19** (3.9)	287 (35.9)
Unknown	20*** (6.5)	0 (0.0)	20 (2.5)

92% assigned to CT, received

100% assigned to no CT, did not receive

Overall no significant difference in toxicity between different chemo regimens

CONCLUSIONS

1. Logistics feasible (>4500 pts enrolled!)
2. More low risk cancers: Change in biology of breast cancer and/or due to screening. This does not affect discordancy rates required for primary aim randomization
3. Clinicians & patients comply with the protocol in the “70-gene signature /genomic arm”.
4. Statistically significant difference in reduction in Chemotherapy administration.

The 70-Gene Signature:

1. Has been validated in terms of prognostication and adds to conventional criteria
2. It has also been validated for $T_{1\text{-}3}N_1$ tumors and for elderly patients
3. The assay is stable and reliable (FDA)
4. There are strong indications that the good-prognosis profile is associated with decreased chemotherapy benefit

Using a good-prognosis 70-Gene Signature to withhold adjuvant chemotherapy in clinically low- to moderate risk patients is therefore justified

2010年11月20日 NCCN/JCCNB Seminar in Japan 開催のお知らせ New 当日のプログラムを下記に掲載いたしました。

＜ テ ー マ ＞ 治療効果予測と予後予測～乳がんのターゲット治療の模索～
乳がんにおける予後及び治療効果の予測検査法について、欧・米・東アジアからの招聘者と共に検討する国際セミナーです。

＜ 場 所 ＞ 東京国際フォーラム ホールB5

Thank you for your attention & discussion & inviting me JCCNB, Dr Seigo Nakamura

Paik et al, JCO, 2006 OTDX Predictive Data based on NSABP B-20 Archival FFPE Blocks

Multigene Predictor for Chemotherapy Response in Breast Cancer

Table 1. Kaplan-Meier Estimates of the Proportion of Patients Free of Distant Recurrence at 10 Years for Tamoxifen-Treated Patients and Tamoxifen Plus Chemotherapy-Treated Patients

		Tamoxifen			Tamoxifen Plus Chemotherapy		
Group	No. of Patients	10-Year DRF (%)	95% CI	No. of Patients	10-Year DRF (%)	95% CI	No. of Patients
All patients	651	87.8	83.3% to 92.3%	227	92.2	89.4% to 94.9%	424
Low risk (RS < 18)	353	96.8	93.7% to 99.9%	135	95.6	92.7% to 98.6%	218
Intermediate risk (RS 18-30)	134	90.9	82.5% to 99.4%	45	89.1	82.4% to 95.9%	89
High risk (RS ≥ 31)	164	60.5	46.2% to 74.8%	47	88.1	82.0% to 94.2%	117

NOTE. Results are given for all patients and for the pre-specified Recurrence Score risk categories.
Abbreviations: DRF, distant recurrence free; RS, recurrence score.

The "High Risk" Tam only arm contained only 47 patients whose OS and DDFS was the metric for comparison with Tam plus Chemorx benefit —a very small group.

Paik et al. *J Clin Oncol*. 2006;24:3726-3734

TargetPrint, single gene read out ER/PR/HER2

ER	IHC pos	IHC neg
MA pos	309	16
MA neg	9	62

PR	IHC pos	IHC neg
MA pos	194	48
MA neg	29	108

HER2	IHC pos	IHC neg
MA pos	50	10
MA neg	8	342

N=~400	ER	PR	HER2
Accuracy	0.94	0.80	0.96
Sensitivity	0.97	0.87	0.86
Specificity	0.80	0.69	0.97

Conclusions:

- Very high concordance between microarray and IHC or FISH for ER and HER2
- Accurate read-out of ER, PR and HER2 on microarray

reference