ESMO 2012
Poster Discussion Session
early breast cancer

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As member of advisory boards and as speaker during satellite symposia, I have received honoraria from Agendia and Genomic Health

Contents

- **We will review and discuss the results of four studies investigating new/already known tools to characterize prognosis in early breast cancer and to determine sensitivity to systemic therapies**

Prognosis

- **a set of eight mi-RNAs**

  (by Ciruelos E et al – abs 250 PD)

- **Mammaprint®**

  (by Cusumano G et al, abs 251 PD)

- **Oncotype Dx®**

  (by Albanell J et al, abs 252 PD)

Prediction of response to HT

- **a set of 3-4 proteins**

  (by Hennessy B et al – abs 249 PD)

Discussion of abstract 249 PD (by Hennessy B et al)

Proteomic predictors of outcome in early breast cancer patients treated with adjuvant tamoxifen. Methods

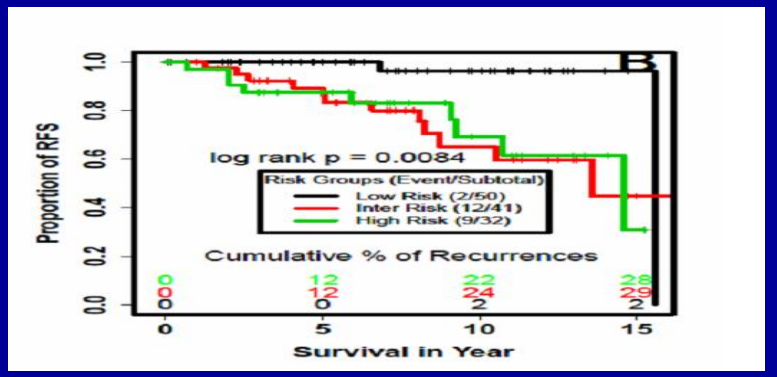
- **Training set: 197 pts. (38% N+)**
  - **Reverse phase protein array (140 antibodies to kinases and steroid signaling proteins)**
  - **Algorythm to predict patient outcomes with a subset of antibodies**
- **Test set: 313 pts. (26% N+)**
  - **AQUA test (immuno-fluorescence-based) to quantify expression of four proteins (Cyclin B1, PAI 1, PgR, BCL2) → correlation with outcome**
- **Additional set: 77 pts. (92% N+)**
  - **Gene expression profile data available to compare the proteomic model with known genomic predictors (Mammaprint®, 76-gene and GGI, H/I, pseudo-21 gene RS)**

Proteomic predictors of outcome in early breast cancer patients treated with adjuvant tamoxifen. Main results

Training set (N=123 pts)

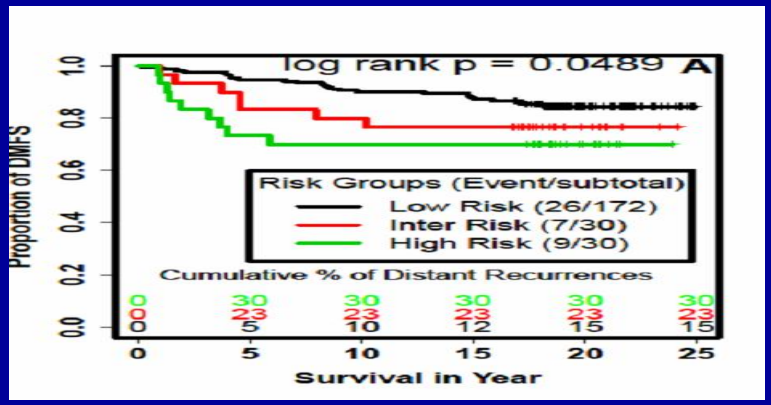
four-protein model

three-protein model

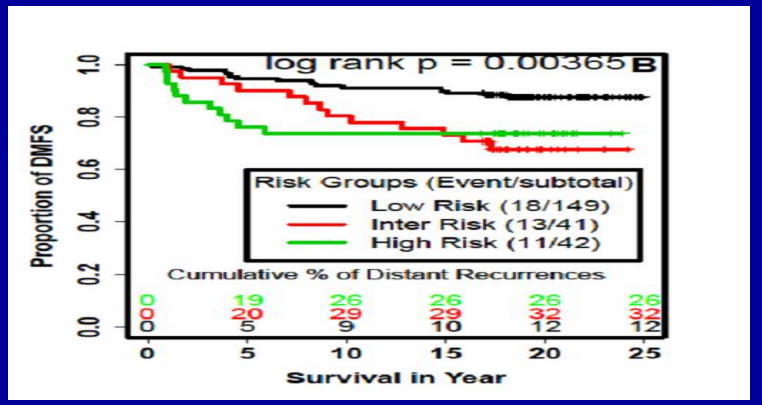


Test set (N=232 pts)

four-protein model



three-protein model



Comparison between the proteomic model and known pathology/genomic predictors

The proteomic model outperformed

Clinical variables

-Grade

-PgR status

-pT

Genomic predictors

-Mammaprint®

-76-gene and GGI signatures

-H/I index

-Pseudo-21 gene recurrence score

in a multivariate analysis

Conclusions

- **The proteomic model might have a future application in the "standard of care" setting because:**

  - **based on proteins, i.e. the immediate effectors of cellular behavior**
  - **performed on a limited number of proteins and on archival samples**

Pending issues

- Patients evaluated in the present study were not treated in the context of a clinical trial

  - heterogeneity in → Follow-up schedules
  - heterogeneity in → Treatment (chemo, duration of TAM, shift to AI)

  ?

  - lack of randomization TAM ± chemotherapy

⇒ Confirmation of the present results on a clinical trial series is recommended

- In the "high risk" group 10-yr. distant metastasis-free survival is 70% (four protein model) or 74% (three-protein model) ⇒ Risk of overtreatment for these pts?

Can the model be improved?

- use more proteins?
- AQUA can also provide information on protein localization within the sub-cellular compartments

Discussion of abstracts 251 PD (by Cusumano P et al) and 252 PD (by Albanell J et al)

Abs 251PD and 252PD: Study characteristics and study design

- **Study design: changes in adjuvant treatment recommendations have been recorded after that the results of the genomic test (Mammaprint® or Oncotype Dx®) were available to a multi-disciplinary team whose original recommendations were based on "standard" clinical-pathological factors**

	Cusumano	Albanell
- Genomic test	Mammaprint®	Oncotype Dx®
- No. pts.	194	527
- Participating countries	B/I/S/N	F/G/S
- % change	22/26/27/33	31.9

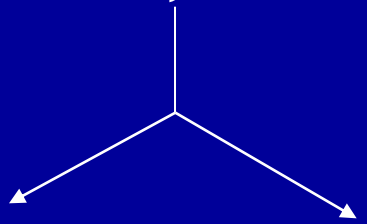
Shared conclusions: ↓ use of chemotherapy, ↑ agreement between centers

Abs. 251PD and 252PD: Points of discussion (1)

% of change in adjuvant treatment recommendation depends on local attitude.

Example:

35 y.o., 2+N, G1, ER+ 90%, PgR+ 70%, Ki-67 5%, HER-2 neg.



Pre-genomic test treatment decision	Center 1	Center 2
	HT alone	CT→HT

It is expected that the treatment decision after the genomic test will change in Center 2 but not in Center 1

Abs. 251PD and 252PD: Points of discussion (2)

- the most important parameter to measure the clinical value of these tests is the demonstration that change in treatment is associated with improved outcome and/or with less treatment toxicity (difficult to demonstrate in a prospectively designed study)

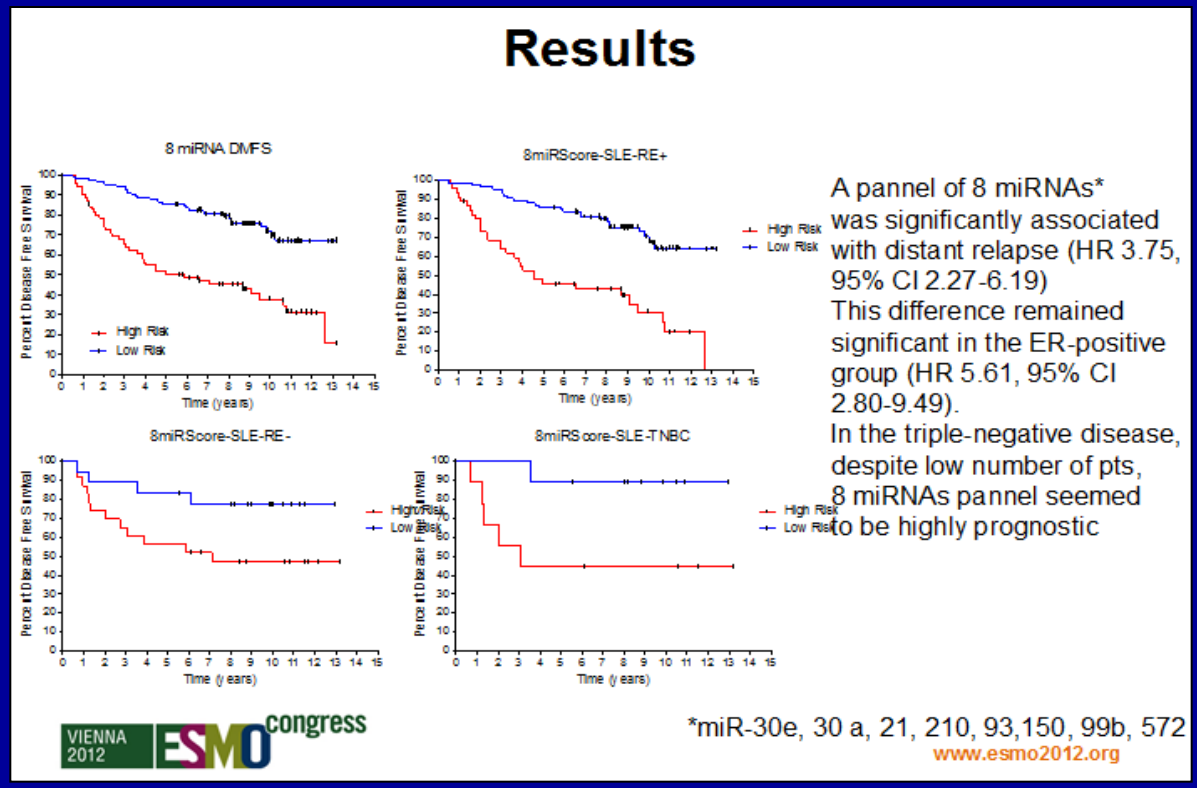
- where these tests could be critical ?
  Patients with ambiguous pathological features: pT1c pNo, G2, ER+ 50%, PgR+ 10%, Ki-67 20%, HER-2 negative

Discussion of abstract 250 PD

(by Ciruelos E et al)

Methods and results

- 173 early breast cancer patients (N+) diagnosed between 1997-2007
- mi-RNA on FFPE samples by TaqMan® (RT-qPCR)
- correlation between mi-RNA levels and clinical outcomes



Points of discussion

- **Justification for the study sample size**
- **Heterogeneity in adjuvant treatments?**
- **Comparison in mi-RNA results between FFPE and FF samples from the same tumor done in 91/173 samples. Criteria for selection?**
- **Each of the eight selected mi-RNAs emerged from a univariate analysis →**
  No specific biological rationale for their use in the prognostic model →
  No biologically driven analysis. Play of chance ?? (additional studies ongoing)

Conclusions

- We have to congratulate the authors for their efforts and for the results of their studies

- In my opinion, none of the presented results is practice-changing; However:
  - tests based on the evaluation of multiple proteins could be more informative than genomic tests to evaluate the level of sensitivity to endocrine-therapy
  - genomic test results may convince physicians to prescribe less adjuvant chemotherapy
  - future studies on mi-RNAs, particularly on their biology in breast cancer, are warranted