Prognostic Significance of Molecular Subtypes in Male Breast cancer

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Background

- About 1% of all breast cancers occur in men
- Cca. 450 cases per year in Germany and 1700 per year in the US
- Current therapy strategies are derived from female breast cancer
- Possible gender specific differences between female and male breast cancer are not sufficiently evaluated

Objective

- to classify the molecular subtypes of male breast cancers based on the expression profile of immunomarkers and to evaluate their association with clinicopathological features and patients outcome

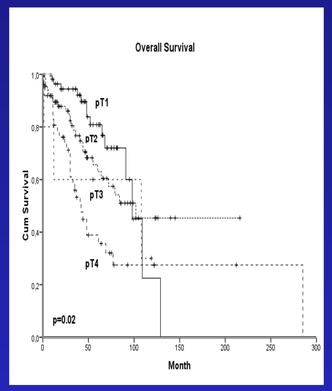
Patients & Methods

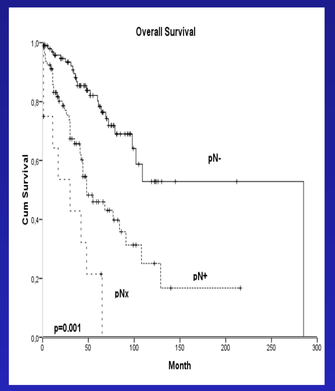
- MBC diagnosed between 1995 and 2007 in region Chemnitz / Zwickau in the State of Saxony, Germany
- Region with 1.5 million inhabitants and 252 inhabitants per km²
- All MBC patients diagnosed 1995-2007 in the region
- Data on tumor characteristics, treatment and follow-up (3 years) was collected by the Cancer Registers of Chemnitz and Zwickau
- To define molecular subtypes a total of 209 cases of male breast carcinoma were examined retrospectively using immunostains for hormone receptors (HR) and cytokeratin 5/6 (CK5/6). Human epidermal growth factor receptor 2 (HER2) expression was evaluated by immunostaining and confirmed by fluorescent in situ hybridization.
- Tumor characteristics and overall survival (OS) data were available and correlated with protein expression and the molecular subtypes.
- Statistical analysis was performed with SPSS for Windows Version 14.0
- A value of $p \leq .05$ was considered statistically significant (Log-Rank test, χ^2 - test)

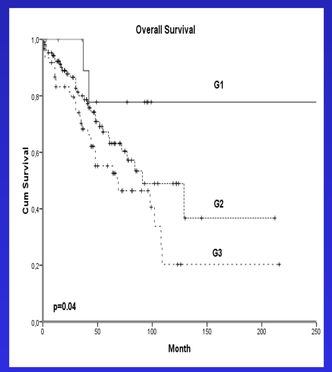
Results

Tab. 1: Patient characteristics

Tumor Characteristics	Cases (%)
Stage	
pT1	62 (29.7)
pT2	71 (34.0)
pT3	5 (2.4)
pT4	60 (28.7)
Nodal Status	
pN negative	105 (50.2)
pN positive	85 (40.7)
unknown	19 (9.1)
Grading	
I	15 (7.2)
II	117 (56.0)
III	67 (33.7)
Hormone Receptors	
negative	19 (9.1)
positive	168 (80.4)
unknown	22 (10.5)
HER2-Status	
negative	160 (76.6)
positive	14 (6.7)
unknown	35 (16.7)







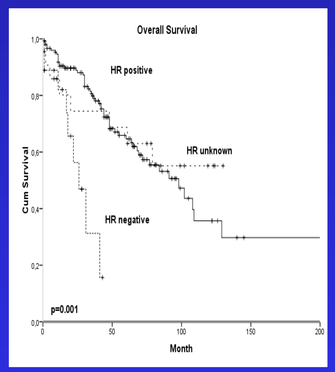


Figure 1: Kaplan-Meier Survival Curves - T-Stadium, Nodal-Stage, Grading, Hormone –Rezeptor (HR)-Status

Tab. 2: Patient characteristics-Molecular subtypes

	Cases (%)
Luminal A (HR+,HER2-)	156 (83.9)
Luminal B (HR-,HER2+)	12 (6.5)
HER2+/HR-	2 (1.1)
Basal-like (HR-,HER2-,CK5/6+)	16 (8.6)

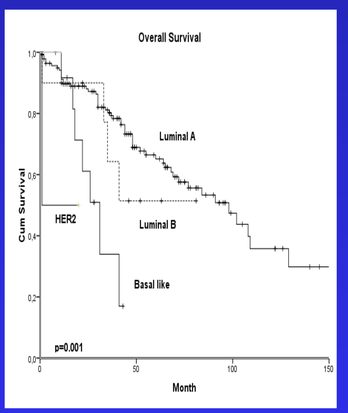


Figure 2: Kaplan-Meier Survival Curves – Molecular Subtypes

- The luminal A subtype (HR+/HER2-) was the most common subtype in male breast cancer (83.9%; n=156) with a median patients OS of 98 month
- Luminal B tumors (HR-/HER+) were found in 6.5% (n=12)
- HER2+/HR- carcinomas in 1.1% (n=2)
- basal-like (HR-/HER2-/CK5/6+) in 8.6% (n=16)
- Basal like male breast carcinoma showed a statistically significant reduced overall survival (median: 32 month; p<0.001)
- Due to the low number of patients prognostic significance of HER2 positivity (luminal B and HER2+/HR-subtype) was not evaluable
- in nodal-negative tumors molecular subtypes showed no statistical overall-survival differences

Summary / Conclusion

- In our study group, luminal A was the predominant subtype of male breast carcinoma and showed an significant inproved patients outcome
- tumors with a basal like subtype which were known to show minor chemotherapy response had a worse prognostic outcome

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