

Improved Survival of HER2-Positive Metastatic Breast Cancer in Routine Care

Rudolf Weide¹, Stefan Feiten², Vera Friesenhahn², Jochen Heymanns¹, Kristina Kleboth², Ulrike Mergenthaler², Jörg Thomalla¹, Christoph van Roye¹ & Hubert Köppler¹

¹ Praxisklinik für Hämatologie und Onkologie, Neversstr. 5, Koblenz 56068, Germany

² Institut für Versorgungsforschung in der Onkologie, Neversstr. 5, Koblenz 56068, Germany

Correspondence: Rudolf Weide, Praxisklinik für Hämatologie und Onkologie, Koblenz, Germany. Tel: 49-(0)261-9215-69323. E-mail: weide@onkologie-koblenz.de

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Abstract

Purpose: Targeted therapy directed against HER2 has improved the outcome of patients with HER2-positive metastatic breast cancer in prospective clinical trials. No data are available how anti-HER2-therapy has influenced survival of unselected patients with HER2-positive metastatic breast cancer who receive treatment in routine care. **Methods:** Data of 118 subsequent patients with HER2-positive metastatic breast cancer who were treated in a community-based oncology group practice between 1995 and 2010 were analyzed retrospectively. **Results:** Median age at initial diagnosis of metastasis was 58 years (33-92). Twenty-two percent were metastasized at diagnosis of breast cancer, seventy-eight percent developed metastases in the course of the disease. Distribution of metastatic sites at initial diagnosis of metastasis was: 23% bone, 58% visceral, 5% CNS, 10% lymph nodes, 4% other. Hormone receptor was positive in 68% and negative in 31%. Palliative treatment consisted of antihormonal therapy in 56%, chemotherapy in 90% and radiotherapy in 50%. Seventy-five percent received anti-HER2-therapy consisting of trastuzumab in 80% and lapatinib in 1%, 19% received trastuzumab + lapatinib sequentially. Twenty-five percent received no anti-HER2-therapy. Median overall survival since initial diagnosis of metastasis was 34 months (0-277+). **Conclusion:** It could be shown that, compared to historical controls, targeted therapy against HER2 prolongs overall survival of patients with HER2-positive metastatic breast cancer who receive treatment in routine care.

Keywords: HER2, breast cancer, trastuzumab, lapatinib, routine care

1. Introduction

HER2 is a 185 kd transmembrane tyrosine kinase which is overexpressed in 15-18% of primary breast cancer cases (Slamon et al., 1987; Dendukuri, Khetani, McIsaac, & Brophy, 2007). HER2 belongs to a family of tyrosine kinases (HER1, HER2, HER3, HER4). Homodimerization of HER2 with itself or heterodimerization with HER1, HER3 or HER4 activates the intracellular tyrosine kinase leading to the stimulation of cell proliferation via the RAS/MAPK-pathway, inhibition of apoptosis via the PI3K/AKT/mTOR-pathway and promotion of angiogenesis due to VEGF-stimulation (Hudis, 2007). It has been demonstrated that HER2-positive breast cancer cells show increased motility and invasiveness. Overexpression of HER2 has been shown to be a strong negative prognostic factor in breast cancer leading to early visceral and brain metastases (Slamon et al., 1987). HER2-positive metastatic breast cancer has an inferior outcome compared to HER2-negative disease with a median overall survival of 18-20 months (Smith, 2001; Slamon et al., 2001). Trastuzumab is a humanized monoclonal antibody directed against the extracellular domain of HER2. Binding of trastuzumab to HER2 inhibits HER2-dimerization and HER2-activation (Hudis, 2007). Additionally trastuzumab induces antibody dependent cell mediated cytotoxicity (ADCC) by attracting natural killer cells (NK cells) and macrophages which themselves are able to kill trastuzumab-coated HER2-positive tumour cells (Hudis, 2007; Clynes, Towers, Presta, & Ravetch, 2000). Thus trastuzumab is able to kill breast cancer cells by the inhibition of the cell

communication between cell surface and nucleus. Additionally trastuzumab directs the immune system of the patient against breast cancer cells which leads to killing of breast cancer cells by natural killer cells and macrophages of the immune system.

Trastuzumab-mono-therapy has been shown to be effective in first line, and further lines of therapy in patients with HER2-positive metastatic breast cancer (Baselga et al., 1996; Cobleigh et al., 1999; Vogel et al., 2002). Within the pivotal trial first line therapy with trastuzumab prolonged overall survival in combination with anthracycline- or paclitaxel-chemotherapy from 20.3 to 25.1 months compared to chemotherapy alone in HER2-positive metastatic breast cancer (Slamon et al., 2001). Lapatinib is a dual HER1 and HER2 tyrosine kinase inhibitor, which in combination with capecitabine has shown activity in trastuzumab-refractory HER2-positive metastatic breast cancer and brain metastases (Geyer et al., 2006; Lin et al., 2008). To date trastuzumab-mono-therapy, immunochemotherapy with trastuzumab, aromatase inhibitor plus trastuzumab in hormone receptor-positive tumours and lapatinib-capecitabine in trastuzumab-refractory disease and brain metastases respectively are all considered standard treatment options in HER2-positive metastatic breast cancer. Prospective clinical trials have demonstrated a prolongation of overall survival by adding trastuzumab to chemotherapy (Smith, 2001; Slamon et al., 2001; Marty et al., 2005).

On the other hand it is known that less than 2% of patients with metastatic breast cancer, who are older than 60 years, are treated within prospective clinical trials (American College of Physicians, 1999). Data from prospective clinical trials are not transferrable into routine care because a significant percentage of patients is excluded from these trials, for example very old patients, patients with brain metastasis, impaired organ function, significant comorbidities, certain pretherapies or a low performance status. No data are available so far how anti-HER2-therapy might influence overall survival in unselected patients with HER2-positive breast cancer who receive treatment outside clinical trials in routine care. This was the reason for us to ask the question whether anti-HER2-therapy leads to a prolongation of life in unselected patients with metastatic HER2-positive breast cancer who received routine care treatment in a community based oncology practice in Germany?

2. Patients and Methods

This was a retrospective study in unselected female patients with HER2-positive metastatic breast cancer who received routine treatment in an oncology group practice in Germany between 06/1995-12/2010. From the time of first diagnosis of metastatic disease until death or the end of observation within this study all patients were treated on an outpatient basis. Patients stayed in their private environment, mostly within their families and received support from relatives and friends. Within the oncology group practice continuity of care was assured by a constant patient-oncologist-relationship. Apart from relatives and friends patients received psychosocial support from their oncologist, the oncology team, general practitioners, gynaecologists, psychologists, social workers and clergy.

All patients gave written informed consent concerning data analysis and data distribution - since it was a retrospective analysis and the patients have agreed no ethical approval was necessary. Participants had to have at least one distant metastasis at the time of diagnosis of metastatic disease. HER2-positivity was defined as 2+ or 3+ overexpression in immunohistochemistry by DAKO HercepTest; in case of 2+, additional overexpression by fluorescence in situ hybridization (FISH) or chromatographic in situ hybridization (CISH) was required. HER2 was evaluated at the time of metastasis and, if not available, at the time of initial diagnosis of breast cancer. All relevant patient data were extracted from patient files and transferred into a database by experienced study nurses. Statistical analyses using SPSS 19 were conducted by a research associate who was supported by an oncologist. Missing data were retrieved from departments of pathology, gynaecology, radiology, radiotherapy, from community based gynaecologists, general practitioners, patients and relatives. At the time of first breast cancer diagnosis the following data were evaluated: age, menopausal status, stage according to TNM (7th edition, 2010), HER2-overexpression, ER/PR-status, grading, histological type, type of operation, type and duration of adjuvant therapy. At the time of diagnosis of metastatic disease: age, menopausal status, time between first breast cancer diagnosis and metastasis (DFS), site of metastasis, number of metastatic sites. From the time of metastasis until death or the end of observation (12/2010): type and duration of antihormonal therapy, number and duration of palliative therapy lines, type and duration of chemotherapy, type and duration of anti-HER2-therapy (trastuzumab-mono, aromatase-inhibitor + trastuzumab, chemotherapy + trastuzumab, lapatinib-mono, capecitabine + lapatinib, sequential trastuzumab + lapatinib), number of trastuzumab-containing therapy lines, first therapy line containing trastuzumab, trastuzumab/chemotherapy combinations used, bisphosphonate therapy, radiotherapy, type of local therapy of brain metastases, cardiac function under trastuzumab, duration and cause of hospitalization (tumour, comorbidity, therapy), cause of death, place of death. Overall survival was defined as the time between initial diagnosis of metastasis and death or the end of observation (12/2010). Survival analyses

were performed according to the method of Kaplan and Meier using SPSS 19. Descriptive analyses (frequencies), medians and means were computed in SPSS as well, mean differences were tested for statistical significance by analyses of variance (ANOVA) or by independent samples t-tests.

3. Results

One hundred and eighteen consecutive patients with complete data sets were evaluated. Patient characteristics are depicted in Table 1.

Table 1. Patient and tumour characteristics

Median age at initial diagnosis of metastasis (n=118)		
▪ 58 years (33-92)		
Menopausal status at the time of initial diagnosis of breast cancer (n=118)		
▪ premenopausal	n=46	39%
▪ postmenopausal	n=72	61%
Tumour grade (n=126; all tumours)		
▪ grading 1 (G1)	n=4	3%
▪ grading 2 (G2)	n=36	29%
▪ grading 3 (G3)	n=74	59%
▪ grading 4 (G4)	n=2	2%
▪ grading not evaluable (GX)	n=10	8%
Histological type (n=126; all tumours)		
▪ ductal	n=79	63%
▪ lobular	n=16	13%
▪ other	n=12	15%
▪ not evaluable	n=19	15%
Hormone receptor status (n=126; all tumours)		
▪ oestrogen receptor positive / progesterone receptor positive (ER+ / PR+)	n=55	44%
▪ oestrogen receptor positive / progesterone receptor negative (ER+ / PR-)	n=16	13%
▪ oestrogen receptor negative / progesterone receptor positive (ER- / PR+)	n=5	4%
▪ oestrogen receptor negative / progesterone receptor negative (ER- / PR -)	n=38	30%
▪ receptor status not evaluable	n=12	10%
Metastatic status at the time of initial diagnosis of breast cancer (n=118)		
▪ no distant metastases (M0)	n=89	75%
▪ distant metastases (M1)	n=26	22%
▪ metastatic status not evaluable (MX)	n=3	3%
Median Disease Free Survival [DFS] (n=118)		
22 months (0 – 362)		
Number of metastatic sites at initial diagnosis of metastasis (n=118)		
▪ mean +/- standard deviation	1.4 +/- 0.72	
▪ median (range)	1 (1 – 4)	
Organ site involvement at initial diagnosis of metastasis [multiple responses possible] (n=118)		
▪ bone	n=43	36%
▪ liver	n=43	36%
▪ lung	n=29	25%
▪ lymph nodes	n=20	17%
▪ pleura	n=8	7%

▪ skin	<i>n</i> =6	5%
▪ brain	<i>n</i> =5	4%
▪ other	<i>n</i> =12	10%
Adjuvant therapy (n=118)		
▪ chemotherapy + antihormonal therapy or chemotherapy + antihormonal therapy + radiotherapy	<i>n</i> =36	31%
▪ chemotherapy or chemotherapy + radiotherapy	<i>n</i> =25	21%
▪ radiotherapy	<i>n</i> =13	11%
▪ antihormonal therapy or antihormonal therapy + radiotherapy	<i>n</i> =9	8%
▪ no adjuvant therapy	<i>n</i> =35	30%

Twenty-two percent of patients were metastasized at the time of first breast cancer diagnosis. The median disease free survival [DFS] was 22 months (0-362), defined as time between initial diagnosis and diagnosis of metastasis. Three percent received trastuzumab in addition to their adjuvant therapy.

3.1 Palliative Systemic Therapy

Seventy-eight percent of patients with hormone receptor positivity received antihormonal therapy (*n*=62) using an aromatase inhibitor in the majority of cases (*n*=50; 81%). Ninety percent of patients (*n*=106) received chemotherapy with a median of 3 chemotherapy lines (0-13).

Seventy-five percent (*n*=89) received anti-HER2-therapy consisting of trastuzumab in 80%, lapatinib in 1% and sequential trastuzumab + lapatinib therapy in 19%. Twenty-five percent (*n*=29) received no targeted anti-HER2-therapy. 2% (*n*=2) had no palliative treatment and 23% (*n*=27) received no trastuzumab. A median of 1 trastuzumab-containing line (0-8) was applied to all patients. Trastuzumab was applied as monotherapy in 37% (10% maintenance therapy) and in combination therapy in 63% of trastuzumab containing therapies. Trastuzumab containing therapy lines and trastuzumab combination partners are shown in Table 2.

Table 2. Palliative trastuzumab therapy

Palliative therapy lines containing trastuzumab (n=88)		
▪ 1 st line	<i>n</i> =33	38%
▪ 2 nd line	<i>n</i> =24	27%
▪ 3 rd line	<i>n</i> =10	11%
▪ 4 th line	<i>n</i> =14	16%
▪ 5 th line	<i>n</i> =5	6%
▪ 6 th line	<i>n</i> =2	2%
Palliative therapies containing trastuzumab (n=217)		
▪ <i>Trastuzumab</i> : mono or maintenance	<i>n</i> =81	37%
▪ Paclitaxel + <i>Trastuzumab</i>	<i>n</i> =39	18%
▪ Vinorelbine + <i>Trastuzumab</i>	<i>n</i> =36	17%
▪ Capecitabine + <i>Trastuzumab</i>	<i>n</i> =17	8%
▪ Docetaxel + <i>Trastuzumab</i>	<i>n</i> =15	7%
▪ Gemcitabine + <i>Trastuzumab</i>	<i>n</i> =12	6%
▪ Docetaxel + Carboplatin + <i>Trastuzumab</i>	<i>n</i> =5	2%
▪ Lapatinib + <i>Trastuzumab</i>	<i>n</i> =2	1%
▪ Lapatinib + Capecitabine + <i>Trastuzumab</i>	<i>n</i> =2	1%
▪ Other + <i>Trastuzumab</i>	<i>n</i> =8	4%

Fifty percent of patients developed bone metastases in the course of the disease, 93% of them received bisphosphonates.

3.2 Palliative Therapy of Brain Metastases

Five percent of patients showed CNS involvement (primary brain metastases) at initial diagnosis of metastatic disease, 35% developed brain metastases during the course of their disease. Twenty percent of these patients showed at initial diagnosis of brain metastases a single metastasis, 71% showed two or more metastases and in 10% the number of metastases was not retrievable. Local therapy consisted of whole brain radiotherapy in 63%, operation plus whole brain radiotherapy in 17%, operation only in 7% and no local therapy in 12%. Twenty-seven percent of the patients who developed brain metastases received lapatinib treatment.

3.3 Hospitalisation and Place of Death

Eighty-three percent of patients had to be hospitalized during the course of treatment. Median number of hospitalizations per patient was 2 (0-11) and the median duration of hospital stay was 8 days (0-79). Causes for hospitalization were induced by the tumour in 67%, comorbidity in 18%, rehabilitation in 13% and side effects of the therapy in 2%. Seventy-nine percent of the patients have died, 86% of these died due to tumour progression and 5% due to other causes. In 9% the cause of death could not be determined. Forty-eight percent of patients could die at home, 35% died in hospital, 3% in an old pensioner's home and 3% in hospice care. In 10% the place of death could not be determined.

3.4 Survival

Median overall survival since initial diagnosis of metastasis was 34 months (0-277+) (Figure 1). The probability of 1, 3, 5, and 10 year survival was 85%, 47%, 25% and 9% respectively.

The presence of CNS metastases at initial diagnosis and a disease free interval less than 2 years were correlated significantly with poor survival (Figure 2 and Figure 3). Univariate analysis showed no significant correlation between different metastatic sites at initial diagnosis, primary metastatic disease, hormone receptor status or anti-Her2-therapy.

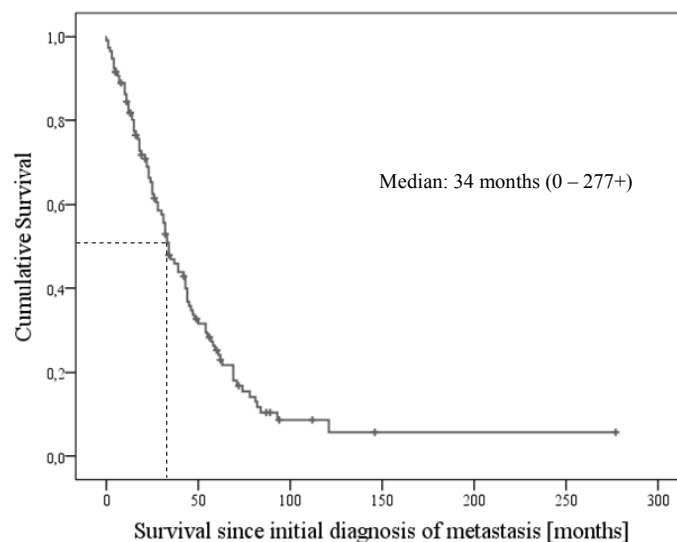


Figure 1. Survival since initial diagnosis of metastasis in months (n=118)

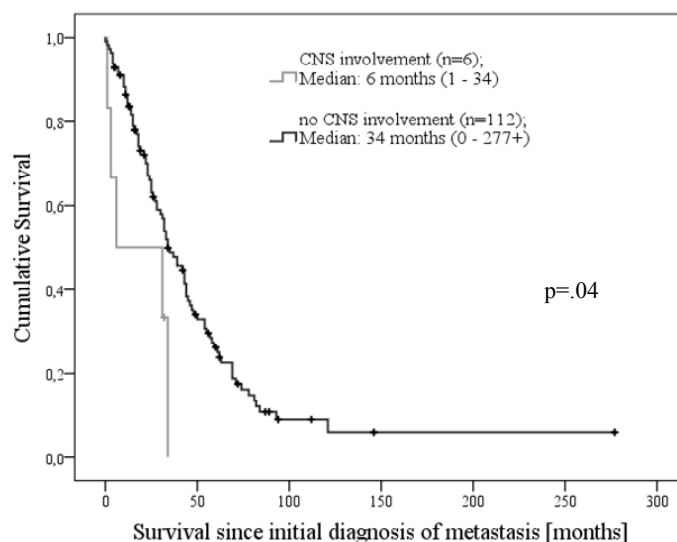


Figure 2. Correlation of survival rates and the presence of CNS metastases at initial diagnosis

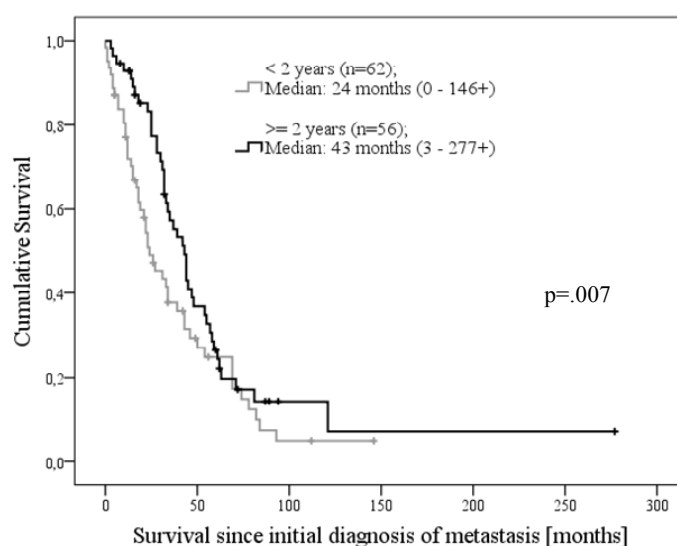


Figure 3. Correlation of survival rates and disease free intervals of more or less than 2 years

Twenty-seven patients with bone metastases only at diagnosis showed a median survival of 39 months, compared to 30 months of 68 patients with visceral metastases. The shortest median survival of 6 months was seen in 6 patients presenting with brain metastases at diagnosis.

Patients with a positive hormone receptor had a median survival of 39 months compared to 27 months in patients who had hormone receptor negative tumours ($p=0.121$). These differences were not statistically significant probably due to low patient numbers.

Table 3 shows characteristics of patients receiving anti-Her2-therapy versus patients receiving no anti-Her2-therapy. The comparison of these groups shows that patients without anti-Her2-therapy fell into a better prognostic subgroup, due to a higher percentage of hormone receptor expression, a lower rate of brain metastases, a lower rate receiving chemotherapy, a higher rate of antihormonal therapy and no palliative therapy at all! Median overall survival was 34 months in patients with anti-Her2-therapy compared to 30 months in patients without anti-Her2-therapy although not statistically significant!

Table 3. Palliative trastuzumab therapy

	anti-Her2-therapy (n=89)	no anti-Her2-therapy (n=29)
Time of diagnosis of metastasis		
▪ 1995 - 1999	24%	24%
▪ 2000 - 2004	48%	48%
▪ 2005 - 2010	28%	28%
Age at diagnosis of metastatic disease		
▪ median (range)	58 (33-92)	63 (39-89)
Disease free interval in months		
▪ median (range)	22 (0-362)	22 (0-247)
Menopausal status at initial diagnosis of metastasis		
▪ premenopausal	29%	21%
▪ postmenopausal	71%	79%
Hormone receptor status: positive		
▪ frequencies	61%	90%
Number of metastatic sites in the course of the disease		
▪ 1 site	26%	38%
▪ 2 sites	29%	41%
▪ 3 sites	22%	21%
▪ more than 3 sites	22%	0%
Metastatic sites in the course of the disease		
▪ CNS	43%	17%
▪ visceral	45%	45%
▪ lymph nodes	4%	17%
▪ bone only	6%	21%
▪ other	2%	0%
Taxane-containing therapies in the course of the disease		
▪ frequencies	75%	31%
Number of palliative therapy lines		
▪ median (range)	5 (1-13)	2 (1-8)
Palliative therapies		
▪ chemotherapy+antihormonal therapy or chemotherapy+antihormonal therapy+radiotherapy	47%	55%
▪ chemotherapy or chemotherapy + radiotherapy	49%	14%
▪ antihormonal therapy or antihormonal therapy + radiotherapy	2%	21%
▪ others	1%	3%
▪ no palliative treatment	0%	7%
Cumulative duration of hospitalizations in days		
▪ median (range)	19 (0-153)	13 (0-154)
Causes of hospitalizations per patient		
▪ tumour	74%	59%
▪ side effects of the treatment	4%	3%
Deaths until the end of observation		
▪ frequencies	82%	69%
Causes of death		
▪ tumour	88%	80%
▪ others	12%	20%
Places of death		
▪ at home	51%	40%
▪ hospital	34%	40%
▪ others	16%	20%

4. Discussion

HER2-overexpression confers a negative prognosis with an increased relapse rate and reduced overall survival in primary breast cancer. Due to the aggressiveness of the tumour, HER2-positive metastatic breast cancer has a significantly shorter median Overall Survival (OS) of 18-20 months compared to HER2-negative disease with a median survival of 24-30 months (Slamon et al., 1987; Smith, 2001; Slamon et al., 2001; Marty et al., 2005). OS has been shown to increase slowly over the years in metastatic breast cancer in prospective studies and in routine care (Gennari, Conte, Rosso, Orlandini, & Bruzzi, 2005; Giordano et al., 2004; Weide et al., 2009). The addition of trastuzumab to anthracycline- or paclitaxel-based first line chemotherapy has improved median OS from 20.3 to 25.1 months (Slamon et al., 2001). A retrospective study has shown that early application of trastuzumab in HER2-positive metastatic breast cancer achieves the same OS as standard therapy in HER2-negative disease (Dawood, Broglio, Buzdar, Hortobagyi, & Giordano, 2009). The difference in prognosis is equalized through the use of trastuzumab (Dawood et al., 2009). The small molecule Lapatinib has the advantage that it has also shown efficacy in brain metastases which developed during trastuzumab therapy (Lin et al., 2008).

The above mentioned studies have shown an improvement of overall survival in HER2-metastatic breast cancer, when trastuzumab is added. It is known that less than 2% of patients with metastatic breast cancer older than 60 years are treated in prospective clinical trials (American College of Physicians, 1999). No data are available that report the percentage of patients with metastatic breast cancer in Germany who receive part of their treatment in prospective clinical trials. In our own group practice only 10% of all patients with metastatic breast cancer are treated in prospective clinical trials due to different reasons (inclusion and exclusion criteria, lack of studies, patient preferences etc). Therefore the impact of anti-HER2-therapy on the majority of patients treated outside clinical trials is not known. In our retrospective study we have observed a prolonged OS of 34 months since initial diagnosis of metastasis in HER2-positive metastatic breast cancer in patients who were treated outside clinical trials in routine care. 75% of patients received trastuzumab therapy as monotherapy or with different chemotherapy partners as combination therapy. Trastuzumab monotherapy has shown efficacy in the first line and in further lines of therapy (Baselga et al., 1996; Cobleigh et al., 1999; Vogel et al., 2002). In hormone receptor positive disease it can effectively be combined with an aromatase inhibitor (Kaufmann et al., 2009). This chemotherapy-free strategy is particularly beneficial for patients who refuse chemotherapy or who have a reduced performance score. In combination therapy it has been shown that different chemotherapeutics like platinum derivatives, taxanes and vinorelbine act synergistically with trastuzumab (Geyer et al., 2006; Pegram et al., 1999; Pietras et al., 1994). Even if the tumour progresses, there is evidence that it is reasonable to continue with trastuzumab while changing the chemotherapeutic partner. This so called treatment beyond progression has shown a prolonged progression free interval compared with a trastuzumab free therapy (von Minckwitz et al., 2009). Concerning lapatinib, 14% of our patients were treated with lapatinib + chemotherapy after trastuzumab due to tumour progression. Especially the combination of lapatinib plus capecitabine has shown efficacy in HER2-positive disease which progresses during trastuzumab treatment (Geyer et al., 2006). Five percent of our patients presented with CNS involvement at initial diagnosis and 35% developed brain metastases during the course of their disease. Treatment consisted mainly of whole brain radiotherapy (WBR) in 63% and operation plus WBR in 17%. The approval of lapatinib for the treatment of brain metastases in HER2-positive breast cancer has improved treatment options in this difficult clinical situation (Lin et al., 2008). Twenty-seven percent of our patients with brain metastases received therapy with lapatinib. Compared to historical controls we have observed an improved median survival of 34 months in our routine care patient cohort, despite the fact that only 75% of the patients received an anti-HER2-targeted therapy. The comparison between patients receiving anti-HER2-therapy and those not receiving this therapy disclosed that patients without anti-HER2-therapy fell into a favourable prognostic group due to a different tumour biology with a lower incidence of CNS involvement, a lower number of metastatic sites in the course of the disease, lower number of palliative lines, lower percentage of patients receiving chemotherapy a higher rate of antihormonal therapy only and a higher rate of no cytoreductive therapy at all (Table 3). Despite less intensive therapy, these patients showed no statistically significant difference in survival (34 versus 30 months). We would like to speculate that if these patients would have received anti-HER2-therapy, the treatment results could have been further improved. Another way of further improving treatment results is looking at the percentage of patients receiving anti-HER2-therapy as part of their first line treatment. Only 28% of our patients received trastuzumab therapy as part of their first line treatment. We would like to speculate that if targeted therapy against HER2 is part of first line treatment, outcome could be improved even further. In summary our data show that anti-HER2-therapy leads to a prolongation of life with a median overall survival of 34 months compared to historical data which have reported a median overall survival of 18-20 months without anti-HER2-therapy (Smith et al., 2001; Slamon et al., 2001). In our own patient cohort of 632 patients with metastatic breast cancer treated in our group practice between

1995-2010 no difference in overall survival could be detected between HER2-negative and HER2-positive patients (Weide et al., 2012c). These observations are in line with data from another institution (Dawood et al., 2009).

Future strategies include the combination of trastuzumab plus lapatinib which has shown superiority over lapatinib in trastuzumab refractory disease (Blackwell et al., 2010). New monoclonal antibodies like pertuzumab, which inhibits HER2-dimerization more effectively and acts synergistically with trastuzumab hold promise (Baselga et al., 2010). Recently data have been presented showing a marked improvement in progression free survival from 12.4 to 18.5 months when trastuzumab and pertuzumab are applied together with docetaxel compared to trastuzumab+docetaxel alone as first line therapy in HER2-positive metastatic breast cancer (Baselga et al., 2011).

Another approach is TDM-1, where the microtubulus-inhibiting drug maytensin is linked to trastuzumab. Upon binding to HER2, TDM-1 is internalized in the cell, maytensin is released and cell killing is achieved by microtubulus inhibition. TDM-1 has shown to be highly active in trastuzumab refractory breast cancer patients (Burris et al., 2011). The development of more potent tyrosine kinase inhibitors might improve specificity and the magnitude of HER2-positive cell killing.

Apart from anti-HER2-therapy we think that the human factor plays a major part in the care of patients with metastatic breast cancer concerning longevity and quality of life. A number of studies have shown that a good psychosocial support not only achieves a better life but also a longer life in metastatic breast cancer and other solid tumors (Spiegel, 2012). We think that the fighting spirit between the patient and her oncologist and the supporting network of the oncology team, relatives, friends, general practitioners, gynaecologists, psychologists, social workers and clergy are a solid basis to reduce psychosocial distress, maintain quality of life and achieve longevity in patients with metastatic breast cancer who receive their treatment in an oncology group practice (Mergenthaler et al., 2011; Weide et al., 2012a; Feiten et al., 2011; Weide et al., 2012b).

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