

REVIEW ARTICLE

Recurrent Breast Cancer

Treatment Strategies for Maintaining and Prolonging Good Quality of Life

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SUMMARY

Background: Recurrent breast cancer remains a challenge for interdisciplinary treatment even though new therapeutic options are available.

Methods: The PubMed database was selectively searched for articles that appeared from 1999 to 2009 and contained the key words „breast cancer,“ „recurrence,“ „metastatic,“ „advanced,“ and „treatment“. Further sources consulted for this review included the German S3 guideline, the treatment recommendations of the German AGO-Mamma group, the NCCN guidelines, and the Cochrane database.

Results: Locoregional recurrences are treated with curative intent. Metastatic breast cancer must be treated on an individualized basis: The treatment should be continued as long as its benefits for the individual patient outweigh its adverse side effects. Endocrine treatment is indicated for all patients whose tumors are hormone-receptor positive or of unknown receptor status and who have enough time for a response to be seen. Chemotherapy should be given if the tumor is hormone-receptor negative, if a rapid response is urgently needed, or if endocrine treatment has failed to produce a response. Combination chemotherapy improves response rates and prolongs progression-free survival, yet it does not prolong overall survival in comparison to monotherapy. In HER2-positive patients, first-line treatment with trastuzumab and monotherapy prolongs overall survival. Other treatment options include angiogenesis inhibitors, various tyrosine kinases inhibitors, radiotherapy, bisphosphonates, surgical or other ablative treatment of metastases, or a combination of these approaches, applied either simultaneously or consecutively.

Conclusions: While locoregional recurrences of breast cancer should be treated with curative intent, breast cancer with distant metastases is currently not curable. It is treated with the intention of restoring and maintaining good quality of life and relieving symptoms due to the metastases, rather than prolonging survival.

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At present around 40% of all patients with breast cancer suffer a recurrence; most of them die from it (1, e1–e3). Breast cancer thus remains the most common cause of cancer-related death in women. The risk of recurrence is highest in the first 2–3 years and then decreases continuously, although it never reaches zero (e4). Ten percent to 20% of all recurrences are isolated locoregional recurrences, while 60% to 70% are distant metastases in one “anatomical structure,” or else in multiple locations (2, e4). The incidence and location of recurrences depend on the initial tumor stage, previous therapy, tumor biology, and the sensitivity of the diagnosis (Table) (1, 3, 4, e5, e6) (Cheang et al.: Breast cancer molecular subtypes and locoregional recurrence. *J Clin Oncol* [Proceedings of ASCO] 26, [May 20 Suppl; Abstr 510] 2008). This article will give a systematic overview of treatment for recurrent breast cancer.

Materials and methods

A selective literature search was carried out in the PubMed database using the search terms “breast cancer” and “recurrence,” “metastatic,” “advanced,” and “treatment” for the period from 1999 to January 2009. Contributions to international congresses on breast cancer in 2008 (ASCO, American Society of Clinical Oncology; SABCS, San Antonio Breast Cancer Symposium; ECCO, European Cancer Organisation; EBCC, European Breast Cancer Conference) were also included. The current German S3 Guidelines (5), the treatment recommendations of AGO-Mamma (the Breast Group of the German Gynecological Oncology Working Group, the *Arbeitsgemeinschaft Gynäkologische Onkologie, Organgruppe Mamma*) (6) and the American NCCN (National Comprehensive Cancer Network) Guidelines (7) together with the Cochrane Database (8) were also included. The statements were evaluated—if this had not already been done in the guidelines themselves—according to the Oxford criteria (evidence level, EL) (e7) and the AGO recommendation grades (Box 1).

General recommendations

Since hormone-receptor expression and *HER2* expression can change in the course of metastasization, determination of receptor status should always be carried out when recurrence occurs, if reasonably possible (EL 1/A AGO-GR++) (e8). In order to detect any further metastases, a re-staging procedure is

TABLE

Location and incidence of metastases found clinically and at autopsy in patients with metastatic breast cancer (2, 4)

Location	Clinical findings (%)	Autopsy findings (%)
Brain	5–10%	30–50%
Lung/pleura	15–20%	50–75%
Local/regional	20–40%	30–50%
Heart	<5%	25–40%
Liver	5–15%	50–75%
Bone	20–60%	60–90%
Intra-abdominal	<5%	30–40%
Endocrine/ovaries	<5%	20–40%

BOX 1

Recommendation grades of the Breast Group of the Gynecological Oncology Working Group (AGO-Mamma) (6)

- ++ This therapy or intervention is highly beneficial for patients and should be performed.
- + This therapy or intervention is of limited benefit for patients and may be performed.
- +/- This therapy or intervention is not of benefit for patients but may be performed in individual cases.
- This therapy or intervention can be disadvantageous for patients and ought not to be performed.
- This therapy or intervention has clear disadvantages for patients and should not be performed under any circumstances.

recommended (chest radiography, bone scintigraphy and liver ultrasonography) (EL 5/D AGO-GR++), although this has not been shown to carry any survival advantage for the patient.

Locoregional recurrence

Local disease recurrence (Box 2) is generally treated curatively (9). In some cases it can be difficult to distinguish between a locoregional recurrence and an ipsilateral second tumor. Features suggesting a second tumor—which like primary breast cancer should be treated curatively—are:

- A long interval of time since the first tumor
- A different location in the breast
- Different tumor biology (hormone-receptor status, HER2-receptor status, tumor grade).

Five-year overall survival after an isolated chest wall recurrence is 68%; after intra-breast recurrence it is 81% (e4). Operable breast, chest wall, and axillary

recurrences should be excised with tumor-free margins (EL 2b/A; AGO-GR++). For intra-breast recurrence, mastectomy is regarded as the standard treatment, although in some cases repeat breast-preserving surgery and interstitial radiotherapy may be undertaken (EL 3/C; AGO-GR+/-). The rate of repeat intra-breast recurrence is higher after such treatment (e9), but the significance of this for overall survival is unclear (6). Patients who have not yet received radiotherapy should be offered it (EL 2b/B; AGO-GR+).

Antihormonal therapy after R0 resection of a locoregional recurrence with M0 status has prolonged the interval until a repeat recurrence, but without improving overall survival (EL 5/D; AGO-GR++) (10). No valid study results are available for chemotherapy or trastuzumab therapy after R0 resection of a local recurrence, so that these cannot be definitely recommended at present (EL 3b/C; AGO-GR+/-) (e10, e11). The exception to this is in HER2-positive patients who have not yet received anti-HER2-treatment (trastuzumab or lapatinib); in this group anti-HER2-treatment (trastuzumab or lapatinib) can be recommended (EL 5/D; AGO-GR+).

In patients with R1-resection in whom further resection is not possible, and in other cases of locoregional recurrences (lymph nodes, skin), chemotherapy, monoclonal antibody therapy, radiotherapy (EL 2/B; AGO-GR++) and combinations of these (e.g., simultaneous radiochemotherapy, EL 3b/C; AGO-GR+) may be considered (e12, e13). In patients with M1 status and/or inoperable local recurrence, decisions about palliative surgery must be made on an individual basis (e.g., where there is ulceration, unpleasant odor, or pain) (EL 5/D; AGO-GR+/-) (6).

Metastatic breast cancer

Treatment goals

Because metastatic breast cancer is not curable, the primary goals of therapy are restoration of quality of life, reduction of tumor-related symptoms, and maintenance of the patient’s social environment; prolonging life is secondary to these (EL 1a/A; AGO-GR++). The possibility of increasing the overall survival of patients with metastatic breast cancer has been the subject of debate in recent years (e14). However, prospective and retrospective studies show that the treatment options available at present do improve overall survival (EL 2a) (e15). The median survival of patients with metastatic breast cancer is currently given as 20 to 28 months; it depends heavily on the nature of the metastases and the tumor biology (11, 12, e16–e18).

Treatment monitoring

To monitor the efficacy of antitumor treatment, a “marker lesion” is chosen. This should be monitored with the simplest method of examination—palpation, ultrasonography, or tumor marker evolution (if raised; CA15–3, CEA, or CA-27–29; HER-2 shed antigen, ECD. Tumor response is “objectified” according to the RECIST criteria (response evaluation criteria in solid

tumors), whereby the longest diameter of the target lesion that can be best visualized is monitored over time—depending on the clinical situation, every 2 to 3 months (e19). Side effects must be recognized before they become clinically manifest (e.g., using echocardiography during trastuzumab therapy) (e20).

Available treatments

Currently licensed treatment options have been greatly expanded in recent years (*Box 3*). In the choice of therapy, previous treatments, comorbidities, side effects, and also the expectations and wishes of the patient must all be taken into account (EL 1c/A; AGO-GR++). More significant than the patient’s actual age is the function of her individual organs (bone marrow, kidneys, liver, heart). Dosages should follow those of the trials on which the licensing was based (EL 1c/A; AGO-GR++). All patients should be offered the chance to participate in clinical studies (AGO-GR++).

Primary metastatic breast cancer

The prognosis of primary metastatic breast cancer depends on the location of the metastases, but is generally regarded as poorer than that of secondary metastatic tumors (EL 4/C). In primary metastatic breast cancer, resection with tumor-free margins (tumorectomy, mastectomy) improves 5-year overall survival by 40% to 50% (13, e21, e22). The role of axillary surgery is unclear.

Endocrine (antihormonal) treatment

Today, endocrine treatment is the first line of therapy for all patients with metastatic breast cancer and positive or unknown hormone receptor status whose disease is not at a life-threatening stage (EL 1a/A; AGO-GR++). A delay of 10 to 12 weeks must be allowed for before the endocrine treatment will start to take effect. Extensive visceral metastases, CNS metastases and/or an urgent need for remission (pain) are reasons not to undertake endocrine treatment. Concurrent chemoendocrine therapy (EL 1b/A; AGO-GR– –) must be avoided, as this is no more effective than the separate therapies but has more side effects (14). Endocrine maintenance therapy following a response to chemotherapy improves not only disease-free survival but also overall survival (EL 3/C; AGO-GR++) (e23).

HER2-positive metastatic breast cancer

HER2 status is not in itself a decision criterion for or against endocrine treatment. All endocrine therapies are less effective when there is overexpression of HER2 than when there is not (15). Compared to anastrozole treatment alone the combination of anastrozole with trastuzumab significantly improved the remission rate (20% versus 7%) and the progression-free interval (5 versus 2 months) (EL 2b/B; AGO-GR+/-) (16).

Compared with an aromatase inhibitor alone, in patients not previously treated with trastuzumab, letrozole combined with the dual tyrosine kinase (HER2, EGFR) inactivator lapatinib showed a significantly

BOX 2

Definition of locoregional recurrence (9)

Recurrence of disease:

- In the breast (after breast-preserving therapy)
- In the chest wall (after mastectomy)
- In the ipsilateral/parasternal/infra- or supraclavicular lymph nodes
- In the skin of the chest wall (not breast)
- In the reconstructed breast
- As a second carcinoma (e.g., angiosarcoma)

BOX 3

Current treatment options in metastatic breast cancer

1. Endocrine therapy (tamoxifen, aromatase inhibitors, fulvestrant, gestagens, GnRH analogs)
2. Chemotherapy (anthracyclines, taxanes, capecetabine, vinorelbine, etc.)
3. Monoclonal antibody therapy (trastuzumab, bevacizumab)
4. Tyrosine kinase inhibitors (lapatinib)
5. Bisphosphonates
6. Irradiation
7. Operative/ablative procedures
8. Combinations/sequences
9. Other (VATS pleurodesis) (VATS: video-assisted thoracic surgery)

higher remission rate (15% versus 28%) and a longer progression-free interval (3 versus 8 months; EL 2b/B; AGO-GR+/-) (17).

Nevertheless, the combination of chemotherapy with trastuzumab remains the standard for all HER2-positive patients. Combinations of hormone therapy and trastuzumab should only be considered for selected patients (e.g., with comorbidities or in whom chemotherapy is contraindicated).

HER2-negative metastatic breast cancer

For premenopausal women, the standard treatment is suppression of ovarian function combined with a second endocrine treatment step (aromatase inhibitor, fulvestrant) by analogy to postmenopausal patients (e24–e26). Endocrine treatment in postmenopausal

BOX 4

Endocrine treatment of metastatic breast cancer, depending on previous treatments

1. During or after adjuvant tamoxifen treatment

All third-generation aromatase inhibitors were more effective as first-line treatment in respect of remission rates and progression-free survival than any other endocrine treatment (EL 1a/A; AGO-GR++) (e62). Whether fulvestrant or, depending on the aromatase inhibitor used in first-line treatment, a steroidal (exemestane) or non-steroidal aromatase inhibitor (anastrozole, letrozole) should be used as second-line treatment must be decided individually in each case. No cross-resistances exist, so giving steroidal after non-steroidal aromatase inhibitors, with a clinical success rate of 25% to 47%, has comparable effectivity to giving the same substances in the reverse order (e63–e65).

Exemestane was also effective as third-line treatment, with a 40% rate of clinical success (e66). Reasons for early use of fulvestrant (selective estrogen-receptor downregulator, SERD) are its very good side effect profile (no musculoskeletal symptoms) and its higher clinical success rate (first-line treatment 57%, second-line treatment 46%) (EL 2b/B; AGO-GR+) (e66, e67).

2. During upfront treatment with aromatase inhibitors (adjuvant from the start)

After treatment with non-steroidal aromatase inhibitors, the steroidal aromatase inhibitors and fulvestrant (EL 2b/B; AGO-GR+) were of equal value, with a response rate of 7%, a clinical success rate of 32% of treated cases, and a progression-free interval of 9 months (e69). There are no data relating to the use of tamoxifen in this situation.

3. During treatment with aromatase inhibitors after switch therapy (2 to 3 years tamoxifen followed by aromatase inhibitor)

If there has been a long interval since earlier tamoxifen treatment, tamoxifen would be an alternative to fulvestrant and the non-cross-resistant aromatase inhibitor (EL 4/D; AGO-GR+).

4. During extended therapy with an aromatase inhibitor (5 years tamoxifen followed by aromatase inhibitor)

In situations where data are missing, fulvestrant or the non-cross-resistant aromatase inhibitor would be a treatment option (EL 4/D; AGO-GR+).

patients with metastatic breast cancer depends on which treatment was previously given, and for how long. At present, there are four clinical situations (*Box 4*). After treatment with tamoxifen, aromatase inhibitors, and fulvestrant, gestagens (medroxyprogesterone acetate, megestrol acetate), with their anabolic, analgesic, and euphorizing side effects, show positive effects in patients in the final stage of the disease. Otherwise, endocrine treatment starts again from the beginning (EL 5/D; AGO-GR+).

Chemotherapy and targeted therapy

There are no real predictors of responsiveness to chemotherapy. If chemotherapy is indicated (*Box 5*), it should be continued so long as the therapeutic index is favorable, i.e., so long as the benefit is greater than the side effects (EL 2b/B; AGO-GR+). Disease progression and untreatable side effects are signs that warrant treatment cessation (EL 1c/A; AGO-GR++).

Mono- versus polychemotherapy

A meta-analysis from 1996 that covered 996 patients and two randomized studies (docetaxel, D, versus docetaxel+capecitabine, DC; paclitaxel, P, versus paclitaxel+gemcitabine, PG) compared monochemotherapies to combination chemotherapies (e27–e29). This showed the combination to be superior to the monotherapy in respect of response (D versus DC: 30%

versus 42%; P versus PG: 26% versus 41%), progression-free interval (4 versus 6 months in both cases), and overall survival (D versus DC: 12 versus 15 months; P versus PG: 16 versus 19 months). However, the combination treatments also led to significantly more side effects. These studies did not address the question of sequential administration of the individual substances. In a multicenter three-arm study, 739 patients were randomized to receive doxorubicin, paclitaxel, or both (A, P, AP) (18). When progression occurred, the patients in the monotherapy arms were treated with the substance they had not received so far. The combination gave rise to higher remission rates (A 34%, P 36%, AP 47%) and a longer progression-free interval (A 6 months, P 6 months, AP 8 months), though toxicity was also higher. There were no significant differences in total survival in the three arms (A 19 months, P 22 months, AP 22 months). At present there are few indications that justify combination chemotherapy, especially since there is no guarantee of a survival advantage in comparison to sequential monotherapy with the same substances (e30).

HER2-negative metastatic breast cancer

The first-line treatment with the highest recommendation grade for previously untreated metastatic breast cancer is anthracyclines and taxanes (EL 1b/A; AGO-GR++) (6). Docetaxel appears to be better when given

at 3-weekly intervals and paclitaxel at weekly intervals (6, 19, e31, e32). Many patients have already received anthracyclines and taxanes as adjuvant treatment. If there has been a long period (more than 2 to 3 years) between the adjuvant treatment and metastatic recurrence, it is certainly acceptable to give a taxane or anthracycline. To reduce the risk of cumulative cardiotoxicity, in this situation the liposomal encapsulation of doxorubicin or epirubicin can be used (EL 1b/A; AGO-GR++). When the patient has been previously treated with anthracyclines, taxanes are indicated (EL 1a/A; AGO-GR++); after previous treatment with anthracyclines and taxanes, capecitabine (EL 2b/B; AGO-GR++), vinorelbine, nab-paclitaxel (nanoparticle-albumin-bound paclitaxel, licensed in the USA), and PEG-liposomal doxorubicin are indicated (EL 2b/B; AGO-GR+). Vinorelbine is indicated above all when there are contraindications to treatment with taxanes (e.g., impaired liver function). Cytostatics not licensed in Germany are nab-paclitaxel and ixabepilone (e33–e35) (licensed in the USA; EMEA, the European Medicines Agency, did not approve its licensing in 2008). Ixabepilone works via inhibition of the microtubule system, without the occurrence of cross-resistance with taxanes (e36–e38). For off-label use of ixabepilone, neuropathy and the therapeutic index must be monitored. Neither of these substances requires a solubilizer, so premedication is unnecessary. If polychemotherapy is indicated, anthracycline–taxane combinations are recommended in patients not previously treated with anthracycline (EL 1b/A; AGO-GR++), and combinations of taxanes with capecitabine (EL 2b/B; AGO-GR+) or gemcitabine (EL 2b/B; AGO-GR++) in patients who have previously received anthracyclines (e28, e29).

Vascularization is a necessary part of metastasization. To that extent, inhibition of angiogenesis using the VEGF-specific antibody bevacizumab is a logical therapeutic approach. As first-line treatment in HER2-negative patients, bevacizumab in combination with docetaxel (D, once every 3 weeks) or paclitaxel (P, once a week) led to significantly higher remission rates (D: 63% versus 44%, P: 28% versus 14%) and an increase in progression-free survival (D: 1 month, P: 5 months), although overall survival was not affected (EL 1b/B; AGO-GR+) (20) (Miles et al.: Randomized, double-blind, placebo-controlled, phase III study of bevacizumab with docetaxel or docetaxel with placebo as first-line therapy for patients with locally recurrent or metastatic breast cancer [mBC]: AVADO. Proc Am Soc Clin Oncol 26, abstr. LBA1011. 2008).

The efficacy and side effects of bevacizumab depend on its early use and individual VEGF genotypes (e62). Bevacizumab is licensed for use in combination with taxanes for first-line treatment of HER2-negative metastatic breast cancer.

HER2-positive metastatic breast cancer

Patients who overexpress HER2 benefit from early use of the monoclonal antibody trastuzumab in combination

BOX 5

Indicators for chemotherapy

- Urgent need for remission (aggressive disease progression, symptoms, vital functions at risk)
- Negative hormone receptor status
- When monoclonal antibody treatment is indicated
- When endocrine treatment is followed by no response or by disease progression

with docetaxel or paclitaxel, with a significant increase in median overall survival (D: 23 versus 31 months, P: 20 versus 25 months; EL 1b/A; AGO-GR++) (21, e40). For this reason, trastuzumab in combination with a cytostatic should be offered as first-line therapy to all patients, with the exception of older patients and those with cardiac morbidity (EL 1b/A; AGO-GR++). Monitoring of heart function is obligatory during trastuzumab therapy. If progression occurs during trastuzumab treatment (\pm taxane), the present recommendation is to switch to lapatinib+capecitabine (EL 1c/B; AGO-GR+), since the combination of lapatinib+capecitabine is significantly better than chemotherapy alone in terms of tumor response (29% versus 16%) and progression-free survival (37 versus 20 weeks) (e41, e42). Lapatinib (\pm capecitabine) seems to be effective in the treatment of radiotherapy-resistant brain metastases (EL 2b/B; AGO-GR+/-) (e43). In patients with metastatic breast cancer not previously treated with trastuzumab, the combination of lapatinib+paclitaxel (EL 2b/B; AGO-GR+/-) led to a significant improvement in clinical benefit (69% versus 40%) and progression-free survival (36 versus 25 months) compared to chemotherapy alone, and median overall survival was also increased (105 versus 82 months) (22). Prospective studies on continuing trastuzumab when disease progression occurs during trastuzumab therapy in combination with chemotherapy showed that continuing the antibody treatment and changing the chemotherapy had a significant advantage over chemotherapy alone, leading to a treatment response of 49% versus 25% for the combination (e44). Continuing trastuzumab therapy when disease progression occurs and changing the chemotherapy (EL 2b/B; AGO-GR+) represents an alternative to lapatinib+chemotherapy. Clinical trials are now ongoing into another HER2 monoclonal antibody, pertuzumab (e45).

Bisphosphonates

Bisphosphonates (BPs) are indicated in all patients with bone metastases (EL 1a/A; AGO-GR++). By inhibiting osteoclast activity, BPs lead to bone stabilization, a reduction in serum calcium concentration, and avoidance of skeletal complications (23, e46–e51). BPs are

given in combination with antitumor therapy and should continue to be given after disease progression (EL 5/D; AGO-GR++). The oral and intravenous routes are equally effective (23, e49–e52). Osteonecrosis of the jaw during intravenous administration (EL 2b) can be avoided if dental cleaning and restoration is carried out first, or by oral administration (EL 4/C; AGO-GR+). More recent data suggest that BPs have direct antitumoral and bone-protective effects (EL 1b/A; AGO-GR+) (24). Denusomab (not yet licensed), a subcutaneously administered anti-RANKL (receptor activator of nuclear factor kappaB ligand) antibody, showed a positive effect on bone metabolism with fewer side effects than BP (e53).

Radiotherapy

Irradiation of symptomatic bone metastases leads to an improvement in pain symptoms, in mobility and function, local stabilization, and reduced risk of bone fracture (EL 1a/B; AGO-GR++).

However, in cases where there is spinal compression or risk of fracture, the combination of surgery followed by radiotherapy is superior to radiotherapy alone (EL 3b/C; AGO-GR++) (e54). For this reason, before radiotherapy is started, the question of whether operative stabilization is required should be clarified at a multidisciplinary case conference (e55).

In cases of “small” CNS oligometastases or where there are metastases in an unfavorable (inoperable) location, MRI-guided stereotactic single irradiation (“radiosurgery”) or fractionated irradiation should be carried out (EL 2b/B; AGO-GR++) (e56). After surgery on CNS metastases, percutaneous irradiation of the entire cranium improves local control and overall survival (EL 2b/B; AGO-GR++). Where there are multiple CNS metastases, irradiation of the entire cranium accompanied by antiedema therapy (glucocorticoids) (EL 1a/A; AGO-GR++) or simultaneous radiochemotherapy (temozolomide, topotecan) is an option (EL 3b/C; AGO-GR+/-). For the treatment of skin, lymph node, plexus, and spinal canal metastases, irradiation with or without combined chemotherapy (EL 4/D; AGO-GR+/-) is effective (e12).

Operative/ablative treatment

For patients with “small” oligometastases who are in good general condition and have had a long progression-free interval, operative or ablative procedures (RFA, LITT, cryotherapy) are therapeutic options (EL 3b/C; AGO-GR+/-) that should be carefully weighed in each individual case (e57–e59). It should be pointed out that these results come from case series with highly selected patients. In addition, the effect of growth factors on tumor cells after major invasive procedures is unclear (e60).

Other treatment options

At present there are no recommendations for regional chemotherapy or the use of hyperthermia (EL 3b/C; AGO-GR-). The treatment of choice for pleural

effusion is pleurodesis with talcum and VATS (video-assisted thoracic surgery) (EL 1b/B; AGO-GR++) (25, e61).

Future prospects

In the present authors’ view, metastatic breast cancer will remain a great challenge for physicians and researchers. Although long-term remissions are possible in individual cases today, no treatment will be available in the foreseeable future that can claim to be curative. For this reason the main aim of current treatment for metastatic breast cancer continues to be, as the authors said at the beginning, to restore and maintain quality of life by the alleviation of symptoms caused by metastases.

Conflict of interest statement

Professor Gerber has received lecture fees and reimbursement of travel expenses from Astra Zeneca, Pfizer, Novartis, Roche, GSK, and Sanofi-Aventis. Dr. Reimer has received lecture fees and reimbursement of travel expenses from Novartis, Astra Zeneca, Pfizer, Sanofi-Aventis, and Roche. Professor Freund has received lecture fees and reimbursement of travel expenses from Hoffmann-La Roche, Novartis, Janssen-Cilag, Astra Zeneca, Mundipharma, and Bristol-Myers Squibb.

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KEY MESSAGES

- Locoregional recurrence of breast cancer should be treated curatively.
- With metastatic breast cancer, restoration of quality of life, reduction of tumor-related symptoms, and maintenance of the patient's social environment are the priorities; prolonging life is a secondary aim.
- Multimodal therapies increase remission rates and progression-free intervals.
- Treatment should continue for as long as the benefits are greater than the unwanted side effects.
- All patients should be offered the opportunity to take part in clinical studies.

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REVIEW ARTICLE

Recurrent Breast Cancer

Treatment Strategies for Maintaining and Prolonging a Good Quality of Life

Bernd Gerber, Mathias Freund, Toralf Reimer

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