



# Optimal Supportive Care for Patients With Metastatic Breast Cancer According to Their Disease Progression Phase

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The clinical progression patterns of metastatic breast cancer (MBC) are heterogeneous; patients experience acute and stable phases at different time points. The acute phase consists of rapid progressive symptomatic changes, whereas in the stable phase, patients have relatively low symptom burden. Therefore, personalized interdisciplinary care is essential. The optimal palliative or supportive care in MBC is to provide comprehensive care that is individually prioritized to the patient's disease status. The purpose of this review is to provide a practical guide for oncologists to understand the priorities for supportive care for patients with MBC in the two phases. We note that for better decision making in patient care, performance status should be broadened to consider not only physical status but also psychosocial needs and cognitive condition. We summarize the clinical importance of physical symptom control, psychosocial support, physical activity, nutrition support, and advance care planning. For optimal care, we present palliative or supportive care checklists according to the disease progression phase, combining the limited evidence with expert input. In the acute phase, close monitoring of the patient's status and symptom management take priority. In the stable phase, the focus can shift to maintenance or improvement of physical strength and emotional condition. Finally, we discuss future directions and unmet needs in providing the best supportive care for patients with MBC.

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## INTRODUCTION

The priority of palliative or supportive care for metastatic breast cancer (MBC) varies depending on patients' disease progression status. Since the clinical progression pattern of MBC is heterogeneous, it is imperative to understand patients' disease status and recognize the appropriate needs and timing of care accordingly. In daily oncology practice and at small community hospitals, palliative care specialists are not always available, and general oncologists usually assess care needs. Therefore, oncologists must be familiar with the needs and priorities for primary supportive care at each disease phase.

Guidelines for palliative care have been provided by multiple national or international groups, including the National Comprehensive Cancer Network (NCCN).<sup>1</sup> However, the guidelines include a large amount of information through which to sort and prioritize. A summarized and prioritized checklist is needed for MBC care. The purpose of this review is to provide a practical guide for oncologists to understand when and how to provide supportive care for patients with MBC, prioritized by phase of disease progression, in an individualized comprehensive manner.

## MBC CLINICAL PROGRESSION PATTERNS AND PHASES

Clinical progression patterns of MBC can be categorized into four types: (1) smoldering, (2) gradual, (3) rapid, and (4) de novo poor condition (Fig 1). These progression patterns and how they affect performance status are very heterogeneous. The smoldering pattern involves a very slow progression of disease with long-term asymptomatic features, which is characterized by survival durations of years, sometimes over 10 years. A typical example of the smoldering pattern is nonaggressive hormone receptor–positive breast cancer with nonvisceral metastasis. The gradual pattern involves a gradual progression of the disease over time; patients are usually stable and asymptomatic at the beginning, but with the progression of disease, the symptoms and rate of progression tend to increase. The rapid pattern involves the rapid progression of disease from the beginning of the metastatic stage. It is characterized by a few months' prognosis and severe symptoms. Finally, in the de novo poor condition pattern, patients are already in poor general health at the very beginning of the metastatic stage. We recognize the difficulty to predict the progression type of a patient by assessing the patient at one time point, but awareness to assess the type is important for clinical decision making. Even

### ASSOCIATED CONTENT

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### Data Supplement

Author affiliations and support information (if applicable) appear at the end of this article.

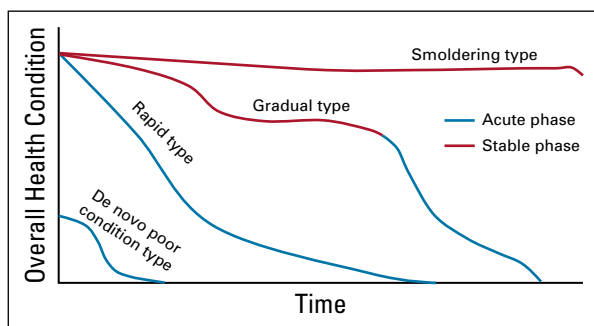
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when the progression type cannot be defined at the first visit, by several visits over a certain period, in most cases, we can generally determine the type.

Each pattern of disease progression has an acute phase and a stable phase at different time points. The acute phase consists of rapid progressive symptomatic changes, whereas in the stable phase, symptoms do not change much. To improve performance status and the overall health condition of patients with MBC, it is necessary to adjust and prioritize care according to these phases. In the acute phase, patients have to focus predominantly on symptom control. By contrast, in the stable phase, they can focus more on the improvement of their health condition by maintaining their physical and emotional condition. We sought to identify detailed strategies for optimal care based on acute and stable phase respectively.

### COMPREHENSIVE ASSESSMENT OF PERFORMANCE STATUS

Performance status, a measure of a patient's functional capacity, is a key consideration in decision making in palliative or supportive care.<sup>2</sup> However, the current performance status assessment tools are focused on physical activity status and do not evaluate nonphysical conditions. For the optimal care of patients with MBC, we also need to assess the psychosocial status and cognitive condition. The well-known tendency of clinicians to focus on physical status more than psychosocial issues can lead to patient preferences and needs going unnoticed. Besides, psychosocial status has been reported to have an impact on the mortality risk for patients in palliative care.<sup>3</sup>



**FIG 1.** Clinical progression patterns of metastatic breast cancer. Clinical progression patterns of metastatic breast cancer can be categorized into four types: (1) smoldering, (2) gradual, (3) rapid, and (4) de novo poor condition. (1) The smoldering pattern involves a very slow progression of disease with long-term asymptomatic features. (2) The gradual pattern involves a gradual progression of the disease over time; patients are usually stable and asymptomatic at the beginning, but with the progression of disease, the symptoms and rate of progression tend to increase. (3) The rapid pattern involves the rapid progression of disease from the beginning of the metastatic stage. (4) The de novo poor condition pattern involves poor general health at the very beginning of the metastatic stage.

For psychosocial assessment, multiple screening tools are available: NCCN Distress Thermometer,<sup>4</sup> Hospital Anxiety and Depression Scale,<sup>5,6</sup> Patient Health Questionnaire,<sup>7</sup> Generalized Anxiety Disorder Screener,<sup>8,9</sup> Brief Symptom Inventory,<sup>10</sup> Impact of Cancer,<sup>11</sup> Cancer Worry Scale,<sup>12,13</sup> and Cancer and Treatment Distress.<sup>14,15</sup> A limitation of these tools is a lack of evidence that supports which screening approach is optimal in clinical practice. A meta-analysis of studies of these and other short screening tools suggested that many have a similar accuracy.<sup>16</sup>

For cognitive condition assessment, clinicians can use either the Mini Mental State Examination or the Montreal Cognitive Assessment.<sup>17</sup> It should be noted that cognitive impairment may be a symptom of a depressive syndrome or fatigue. Incorporating evaluation of psychosocial and cognitive conditions into performance status assessment enables clinicians, as well as caregivers, to provide optimal care to patients.

In summary, it is meaningful to add the assessment of psychosocial and cognitive status to the traditional performance status to evaluate the overall health of patients with MBC. A comprehensive health condition assessment tool should also be developed and validated as to whether it can predict patient survival or outcome. There is an unmet need for a more simplified performance status assessment for oncologists and their staff that reflects emotional status and cognitive function.

### RECOMMENDED SUPPORTIVE CARE AND ASSESSMENT BY PROGRESSION PHASE

In a systematic review,<sup>18</sup> the most common symptoms experienced by patients receiving palliative care included pain, fatigue, dyspnea, nausea, depression, anxiety, and insomnia.<sup>19</sup> A symptom assessment checklist for use with all patients with MBC is summarized in the Data Supplement, online only.

The optimal management for the symptoms in each progression phase, highlighting the roles of both clinicians and patients or caregivers, is summarized in Table 1. Details of pain management are described in two commonly used guidelines for the management of cancer pain, the WHO guidelines<sup>20</sup> and the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) for Adult Cancer Pain.<sup>21</sup> Fatigue management is described in NCCN Guidelines for Cancer-Related Fatigue<sup>22</sup> and the ASCO guidelines.<sup>23</sup>

Below, we will talk about some of the most forgotten topics by healthcare providers, such as distress, exercise, nutrition, and advance care planning, to support patients with MBC.

### Distress and Psychosocial Support

Distress is defined as “a multifactorial unpleasant experience of a psychologic (cognitive, behavioral, and emotional), social, spiritual, and/or physical nature that may

**TABLE 1.** Optimal Symptom Management in Each Progression Phase

<b>Progression Phase</b>	<b>Clinicians' Roles or Responsibilities</b>	<b>Patients' and Caregivers' Roles or Responsibilities</b>
<b>Pain management</b>		
All phases	<ul style="list-style-type: none"> <li>• Perform formal comprehensive assessment or re-evaluate at each visit</li> <li>• Optimize pharmacologic and nonpharmacologic interventions</li> <li>• Psychosocial support</li> <li>• Education for patient and family</li> </ul>	<ul style="list-style-type: none"> <li>• Follow pain plan</li> <li>• Communication with care providers</li> <li>• Monitor pain levels</li> <li>• Contact care providers if pain worsens or side effects are uncontrolled</li> <li>• Coping strategies for distress</li> <li>• Identify patient's goals for comfort and function</li> <li>• Optimized quality of life</li> <li>• Educational tools</li> </ul>
Additional tasks for acute phase	<ul style="list-style-type: none"> <li>• Basic pain control</li> <li>• Refer to palliative or supportive care or pain specialist</li> <li>• Pay attention to uncontrolled pain; rule out oncologic emergency</li> <li>• Nerve block</li> <li>• Palliative radiotherapy</li> </ul>	<ul style="list-style-type: none"> <li>• Obtain assistance from social services</li> <li>• Define realistic goals, revise, and review</li> <li>• Relief of caregiver burden</li> </ul>
Additional tasks for stable phase	<ul style="list-style-type: none"> <li>• Basic pain control</li> </ul>	<ul style="list-style-type: none"> <li>• Personal growth and enhanced meaning</li> <li>• Strengthened relationships</li> </ul>
<b>Fatigue management</b>		
All phases	<ul style="list-style-type: none"> <li>• Perform or re-evaluate by formal comprehensive assessment</li> <li>• Treat contributing factors (pain, anemia, malnutrition, tumor burden, inactivity, insomnia, depression, and other comorbidity)</li> <li>• Consultation with supportive care providers, rehabilitation, and nutrition</li> <li>• Cancer-related fatigue clinic</li> </ul>	<ul style="list-style-type: none"> <li>• Self-monitoring of fatigue or energy levels</li> <li>• Identify patterns of peaks and valleys</li> <li>• Improve sleep hygiene and get adequate sleep</li> <li>• Nonpharmacologic interventions <ul style="list-style-type: none"> <li>○ Physical activity or exercise</li> <li>○ Mind-body interventions <ul style="list-style-type: none"> <li>○ Mindfulness-based approaches, yoga, acupuncture, and massage</li> </ul> </li> </ul> </li> <li>• Find meaning in current situation</li> </ul>
Additional tasks for acute phase	<ul style="list-style-type: none"> <li>• Pharmacologic interventions</li> </ul>	<ul style="list-style-type: none"> <li>• Energy conservation <ul style="list-style-type: none"> <li>○ Plan activities ahead of time to better alternate tasks</li> <li>○ Set priorities</li> <li>○ Delegate or defer activities</li> <li>○ Pacing</li> <li>○ Positioning</li> <li>○ Labor-saving and assistive devices (wheelchairs, walkers, and commodes)</li> <li>○ Schedule important activities at times of peak energy</li> <li>○ Keep naps &lt; 1 hour so as to not interfere with sleep</li> </ul> </li> </ul>
Additional tasks for stable phase	<ul style="list-style-type: none"> <li>• Nonpharmacologic interventions <ul style="list-style-type: none"> <li>○ Psychosocial interventions</li> <li>○ Cognitive behavioral therapy</li> <li>○ Psychoeducational programs</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>• Use distraction <ul style="list-style-type: none"> <li>○ Music, games, and socializing</li> </ul> </li> <li>• Maintain optimal level of activity</li> <li>• Exercise</li> </ul>
<b>Dyspnea management</b>		
All phases	<ul style="list-style-type: none"> <li>• Treat contributing factors (pleural effusion, pneumonia, pulmonary emboli, airway obstruction, anemia, and neuropsychiatric factors)</li> <li>• Psychosocial support</li> </ul>	<ul style="list-style-type: none"> <li>• Breathing techniques</li> <li>• Maximize nutrition</li> <li>• Accommodation strategies (change in living arrangement, frequent rest, and altered activity)</li> <li>• Fan blowing on face</li> <li>• Relaxation</li> </ul>
Additional tasks for acute phase	<ul style="list-style-type: none"> <li>• Pharmacologic intervention (opioids and palliative sedation)</li> <li>• Supplemental oxygen</li> <li>• Noninvasive ventilation</li> </ul>	<ul style="list-style-type: none"> <li>• Energy conservation</li> <li>• Advance activity planning</li> <li>• Position</li> </ul>
Additional tasks for stable phase	<ul style="list-style-type: none"> <li>• Assess need for chronic supplemental oxygen</li> </ul>	<ul style="list-style-type: none"> <li>• Exercise</li> <li>• Distraction strategies (cognitive-behavioral therapy, acupuncture, music, and imagery)</li> </ul>

interfere with the ability to cope effectively with cancer, its physical symptoms, and its treatment.”<sup>24</sup> According to the NCCN Guidelines,<sup>24</sup> screening for distress should be a standard feature of every medical visit, using an NCCN tool, the Distress Thermometer, which asks patients to rate their extent of distress in the past week (1-10 scale), and a list from which to identify practical, family, emotional, physical problems, and spiritual or religious concerns experienced in the past week.<sup>24</sup> For both acute and stable phases of MBC, clinicians should assess risk factors for these issues. If applicable, patients should be referred to mental health professionals, social workers, or chaplains. Patients and caregivers may benefit from NCCN guidelines for patients,<sup>24</sup> counseling, and support groups. For patients with acute-phase disease, coping strategies and improvement in comforting measures are useful. For patients with stable-phase disease, exercise, rehabilitation, meditation, and creative therapies might be helpful. Another important element of psychosocial support is to assess the needs and concerns of the patient’s family and caregivers. Clinicians should pay attention to both the patient and constellation of family and caregivers.<sup>24</sup>

### Physical Exercise

Among the limited studies of physical exercise interventions for patients with MBC, most have focused on early-stage patients and survivors. A systematic review of exercise interventions for patients with advanced cancer demonstrated improvements in aerobic capacity (14 of 19 studies), physical strength (11 of 12 studies), and physical function (nine of nine studies). Fatigue and quality of life were shown to improve in slightly over half of all evaluated studies (11 of 19 studies for fatigue and 10 of 19 studies for quality of life), but all studies suggested improvement in functioning.<sup>25</sup>

For patients in either phase of disease, the balance of feasibility or risk with the efficacy of physical activity is important. If feasible, physical exercise might be a good option for maintaining physical capacity, improving fatigue, and quality of life. For patients with acute-phase disease, clinicians should discuss the safest approach for patients to incorporate exercise into their daily lives. For patients with stable-phase disease, physical exercise may be a suitable approach for maintaining physical capacity. If feasible, obtaining physical therapy, occupational therapy, or personal training might be a good option. However, the evidence that physical exercise improves cancer-related symptoms other than fatigue for patients with MBC remains controversial at present.

A relevant clinical question is whether patients need cardiovascular screening prior to beginning an exercise program. A retrospective analysis of 413 patients who had cancer and cardiovascular risk for exercise suggested that pre-exercise screening was not necessary for most patients with cancer, but should be considered for the following

high-risk patients: (1) patients with a high-risk factor for coronary heart disease (prior anthracycline or cisplatin use and exposure to mediastinal radiation), (2) patients with diabetes mellitus, and (3) patients older than 55 years who are presently sedentary and plan to initiate vigorous exercise.

### Nutrition Support

Nutrition and diet are key lifestyle factors for maintaining quality of life and physical strength, rebuilding tissue damaged by treatment and disease, managing treatment side effects, and preventing infection. Two major aspects are important for patients with MBC: (1) the impact of nutrition on cancer outcomes and (2) how to eat well for quality of life and symptom control.

As for nutrition and cancer outcomes, the evidence is lacking in MBC because most studies have focused on patients with early-stage cancer, survivors, or cancer prevention. In patients with early-stage breast cancer and survivors, the NCCN guideline for breast cancer<sup>26</sup> suggests that healthy diet, limited alcohol intake, and maintaining an ideal body weight (body mass index 20-25) may lead to the best breast cancer outcomes.<sup>26-31</sup> For breast cancer prevention, a Mediterranean diet and soy food intake may have protective effects.<sup>32,33</sup> However, there is no evidence of the impact of nutrition on MBC outcomes at present.

Regarding the role of nutrition in a patient’s quality of life and symptom management, well-balanced nutrition is generally important for body healing and symptom control. Recommended are vegetables, fruits, whole grains (25-30 g of fiber daily), lentils, beans, protein, and plenty of fluids (at least 2 L daily); foods to avoid are extremely high-fat meats, alcohol, sweets, and undercooked foods. It is important to note that a healthy balance of nutrients is crucial, and extreme diets could be harmful. For symptom control of nausea, vomiting, and mouth sores, adapting meals to the situation is warranted. If a patient has difficulty eating, having a consultation with a dietitian will help to introduce more nutrition into the daily diet. Creating a meal plan with a dietitian before symptoms develop is also recommended for a well-balanced nutrition intake. As an example of an adaptive strategy, if a patient has difficulty eating three large meals a day, grazing on smaller portions 5-6 times a day may work better. Snacks such as granola bars, yogurt, and peanut butter on crackers or apples may be favorable. Family and caregivers should understand the patient’s eating patterns. Patients with acute-phase disease should be free to eat whatever they want regardless of nutrition and should not be forced to eat.

### Advance Care Planning

Advance care planning is a process that supports adults at any age or stage of health in understanding and sharing their personal values, life goals, and preferences regarding future medical care.<sup>34</sup> Clinicians should inform patients about their expected possible clinical outcome, prognosis,

treatment options, and helping patients to formulate preferences. The best timing of advance care planning should be at the beginning of the diagnosis of MBC by a multidisciplinary approach, including physicians, social workers, palliative care team, nurses, etc. In advance care planning, clarifying a patient's goal of care is crucial. We should consider how the patient wants to live, to spend his or her time, and to continue or discontinue anticancer treatment.

For patients with stable-phase disease, medical care providers should: (1) assess fears about dying and address anxiety, (2) assess decision-making capacity, (3) initiate discussion of personal values, preferences for end-of-life care, and document them in the medical record, and (4) determine whether the patient has a living will, medical power of attorney, healthcare proxy, or patient surrogate for health care. If not, the patient should be encouraged to complete these tasks. It is recommended for the patient and caregivers to discuss the patient's wishes together and confirm the understanding that MBC is not curable.<sup>1</sup>

For patients with acute-phase disease, medical care providers should: (1) confirm patient and family decisions about life-sustaining treatments, (2) determine patient and caregiver preferences for the location of death, (3) explore caregiver concerns about the patient's plan and seek

resolution of the conflict between the patient's and caregivers' goals and wishes, (4) explore the desire for organ donation or autopsy, and (5) encourage the patient and family to limit use of CPR through do not resuscitate or do not attempt resuscitation or allow natural death orders.<sup>1</sup>

Additionally, in the recent COVID-19 pandemic, vision of advance care planning is rapidly changing. Consideration for the limitation, priority of medical resources, and needs for web-based tools are the key features of advance care planning in this COVID-19 era.<sup>35,36</sup>

### OPTIMAL SUPPORTIVE CARE FOR MBC

Table 2 provides checklists for palliative or supportive care for MBC with consideration of the priorities of acute versus stable phases. In the acute phase, close monitoring of the patient's status and symptom management take priority. In the stable phase, the patient has more time and energy for maintenance or improvement of physical strength and emotional condition through exercise and other wellness activities. Such efforts to maintain and improve quality of life are important in preparation for future acute phases of disease; improvement of physical strength and performance status leads to better survival outcome.<sup>37-40</sup> Because in the acute phase of disease, patients have to focus on the urgent difficulties in front of them, patients and

**TABLE 2.** Checklists for MBC Care With Priorities of Each Phase

Supportive Care Priority	Physicians To Do	Patients or Caregivers To Do
<b>Acute phase</b>		
<ul style="list-style-type: none"> <li>• Close monitoring of performance status and symptoms</li> <li>• Symptom management</li> <li>• Advanced care planning</li> <li>• Social support</li> </ul>	<p>Oncologists to do</p> <ul style="list-style-type: none"> <li>• Basic symptom assessment and management</li> <li>• Cancer treatment decision</li> <li>• Goal setting of care</li> <li>• Basic end-of-life care</li> <li>• Spiritual concerns</li> <li>• Patient and family's understanding of the disease and treatment</li> </ul> <p>Refer (if applicable)</p> <ul style="list-style-type: none"> <li>• Supportive and palliative care specialist</li> <li>• Rehabilitation (PT or OT)</li> <li>• Pain specialist</li> <li>• Social worker</li> <li>• Hospice or nursing care</li> </ul>	<ul style="list-style-type: none"> <li>• Identification of patient's goals for function and comfort</li> <li>• Optimized quality of life</li> <li>• Setting of realistic goals</li> <li>• Relief of caregiver burden</li> <li>• Assessment of safety and accessibility with PT or OT</li> </ul>
<b>Stable phase</b>		
<ul style="list-style-type: none"> <li>• Maintenance or improvement of physical strength and performance status</li> <li>• Psychosocial support</li> <li>• Medical literacy</li> <li>• Advance care planning</li> </ul>	<p>Oncologists to do</p> <ul style="list-style-type: none"> <li>• Basic symptom assessment or management</li> <li>• Cancer treatment decision</li> </ul> <p>Primary care physicians to do</p> <ul style="list-style-type: none"> <li>• General healthcare maintenance</li> </ul> <p>Refer (if applicable)</p> <ul style="list-style-type: none"> <li>• Rehabilitation</li> <li>• Nutritionist</li> <li>• Psychiatrist</li> <li>• Integrative medicine</li> <li>• Social worker</li> </ul>	<ul style="list-style-type: none"> <li>• Exercise</li> <li>• Nutrition</li> <li>• Well being</li> <li>• Emotional wellness</li> <li>• Hygiene control</li> <li>• Medical literacy</li> <li>• Vaccination of caregiver</li> </ul>

Abbreviations: MBC, metastatic breast cancer; PT, physical therapy; OT, occupational therapy.



caregivers must try to maintain or improve their condition while in the stable phase. The team should address advance care planning both in acute and stable phases and to revisit the issues periodically to be incongruent with patient's goals and values.

## FUTURE PERSPECTIVES AND UNMET NEEDS

To provide optimal care for patients with MBC, the integration of oncology and palliative care is crucial. One of the keys to optimal care for patients with MBC is the availability of a palliative oncologist who is dually trained in both palliative care and oncology. The palliative oncologist can develop further communication and collaboration between the oncology and palliative care team, which are necessary for effective integration.<sup>41</sup> They also can take a role in educating oncologists about palliative care, educating palliative care specialists about oncology, and advocating for increased allocation of resources to and greater awareness of supportive care needs.<sup>42</sup>

Two major unmet needs in integrating palliative care into oncology are optimizing referral timing and limitations in the quality of research. To optimize referral timing, a recent focus is creating automatic systems for a referral to palliative care based on standardized criteria.<sup>42</sup> Active efforts are underway to establish evidence for this approach and determine proper standardized referral criteria.<sup>43</sup> Another

aspect commonly overlooked is a routine screening of symptoms to optimize care.

Regarding the quality of research in palliative care, an increasing number of well-conducted studies have been published. However, there is much to improve the quality and quantity of studies, which are more integrated with our clinical oncology care by the primary service.<sup>44</sup> To improve the integration of oncology and palliative care, researchers need to conduct well-designed clinical studies that address clinically meaningful outcomes for all parties involved in the care of advanced cancer. Therefore, a collaboration between oncologists and palliative care specialists is necessary.<sup>42</sup>

In conclusion, the recent evolution in breast cancer treatment and palliative care has altered the clinical courses of many patients with MBC, with some cases rapidly progressing and others smoldering for years. Personalized care requires a focus on when and how and when cancer therapies and supportive measures should be delivered to optimize patient outcomes based on how the disease progresses and whether the patient is in an acute or stable phase and experiencing symptoms or discomfort. As summarized in this review, it is essential to understand that there are several types of clinical progression courses of MBC and to prioritize the focus of care based on acute versus stable phases. To validate efficacy and provide evidence for the optimal supportive care, further well-conducted clinical studies are needed.

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## AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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**AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST****Optimal Supportive Care for Patients With Metastatic Breast Cancer According to Their Disease Progression Phase**

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