A majority of new cancer cases occur in older adults (aged 65 years and older); however, older adult patients often are underrepresented in clinical trials. Because of this, sufficient evidence is lacking for the creation of treatment guidelines for older adult patients. Evidence has shown that many therapeutic agents are effective in both older and younger adult patients. Although efficacy outcomes may be similar, safety profiles may differ by age because of inherent differences in drug metabolism or other reasons. The underrepresentation of older adult patients in clinical trials is explored in this article, along with the current recommendations for treating older adult patients with metastatic breast cancer (MBC). In addition, current evidence from clinical trials and subanalyses of older adult patients with MBC are discussed. Finally, nursing considerations for the management of older adult patients with MBC are provided.

Diana Donovan, ANP

The number of older adult patients (aged 65 years and older) with cancer is rising as the population of the United States ages (Smith, Smith, Hurria, Hortobagyi, & Buchholz, 2009). In a study by Smith et al. (2009), the total incidence of cancer was projected to increase by 45% overall by the year 2030. In addition, by the year 2030, an estimated 70% of all cancers will be diagnosed in older adults (Smith et al., 2009). Aside from female gender, increasing age is the most important risk factor for breast cancer (American Cancer Society, 2012b). About 43% of all new cases of invasive breast cancer were diagnosed in women aged 65 years or older in 2011 (American Cancer Society, 2012a). Although treatment of metastatic breast cancer (MBC) has improved since the early 2000s, meaningful improvements in treatment strategies have not been observed for older adult patients (Tahir, Robinson, & Stotter, 2011). In addition, many older adult patients are undertreated, and some may not be treated at all (Manders et al., 2006). The lack of meaningful improvements in treatment strategies and undertreatment of older adult patients have led to a serious impact on survival outcomes in this patient population (Bastiaanet et al., 2010; Davis, Iyer, & Candrilli, 2011). The five-year relative survival rate is more than 20% for all patients with MBC (Howlader et al., 2012); however, studies have shown that the five-year survival rate is 20% or less for patients aged 65 years or older (Bastiaanet et al., 2010; Davis et al., 2011). Identifying optimal treatment strategies for older adult patients with MBC is, and will remain, of great importance. Unfortunately, many challenges exist in treating older adult patients. In this article, in addition to exploring these challenges, recommendations for treating older adult patients with MBC, clinical outcomes in select trials of older adult patients with MBC, and considerations for nursing practice are discussed.

Treatment Challenges

Older adult patients are a heterogeneous population with multiple factors that can affect the efficacy and safety of chemotherapy. Aging is associated with changes to most body systems—including endocrine, cardiac, gastrointestinal, renal, hepatic, pulmonary, hematologic, immune, musculoskeletal, and neurologic systems—that can impact the efficacy of cancer treatment and increase the risk of toxicities (Sawhney, Sehl, & Naem, 2005; Sehl, Sawhney, & Naem, 2005). Renal function changes are the most significant changes in older adults.
(Aymanns, Keller, Maus, Hartman, & Czock, 2010). Because the kidneys function in drug elimination, decreased renal function can affect the pharmacokinetic (PK)/pharmacodynamic (PD) profile of chemotherapy agents (Aymanns et al., 2010). Changes in PK/PD parameters often are used to consider dosage adjustments; however, dose adjustments may lead to undertreatment if they are calculated incorrectly (Aymanns et al., 2010). Those changes place patients at an increased risk for toxicities, such as nephropathy and volume depletion (Sawhney et al., 2005). Studies have demonstrated decreased total drug clearance in older adult patients versus younger patients with chemotherapy agents such as docetaxel, paclitaxel, epirubicin, etoposide, vinorelbine, and methotrexate (Aymanns et al., 2010). Hepatic mass and liver blood flow also have been demonstrated to decrease with aging (Le Couteur & McLean, 1998; Zoli et al., 1999). Hepatic changes can affect drug metabolism and bioavailability and can increase the risk of drug-related toxicities (McLean & Le Couteur, 2004). Neurologic changes include neuronal loss and decreases in the amount of peripheral nerve myelin (Sehl et al., 2005). Many chemotherapeutic agents are associated with the development of treatment-related neuropathy, which may be worse in older adult patients (Sehl et al., 2005). Changes in hematologic function with age include decreased hemoglobin concentration and decline in bone marrow function (Sehl et al., 2005). Hematologic adverse effects (AEs), such as neutropenia, anemia, and thrombocytopenia, are common with a number of chemotherapeutic agents (Gillespie, 2005). Therefore, many older adult patients are at an increased risk for developing treatment-related hematologic toxicities from chemotherapy (Sehl et al., 2005).

In association with the mentioned age-related body system changes, the course of disease in many older adult patients may be complicated by any number of comorbidities, such as hypertension, diabetes, heart disease, and arthritis (Misra, Seo, & Cohen, 2004; Yancik et al., 2001). In addition to potentially affecting chemotherapy PK/PD, comorbidities increase the likelihood of polypharmacy (multiple concomitant medications) (Extermann, 2006). Comorbidities in older adult patients are associated with higher mortality in patients with breast cancer because the comorbidities increase the risk of death from non-breast cancer-related causes (Yancik et al., 2001). Polypharmacy may increase the risk of drug interactions and may affect the metabolism of another therapeutic agent in some cases (Misra et al., 2004).

Physiologic changes, comorbidities, and polypharmacy are major factors affecting the treatment of older adult patients with MBC; however, a number of other factors also exist. In general, in the older adult population, limited clinical data exist on the efficacy and safety of many therapeutics. The main reason is that older adult patients are underrepresented in a large number of clinical trials (Debled, Bellera, Donamaria, & Souheyryan, 2011). A survey of 156 providers who treated patients with breast cancer indicated several reasons for that underrepresentation (Kornblith et al., 2002). One reason, as described previously, is that older adult patients may have significant comorbid conditions that could affect treatment response. Another reason is that older adult patients may have difficulty comprehending the requirements of a trial, leading to poor adherence. Providers also are concerned about treatment-related toxicities in older adult patients. In addition, older adult patients often do not meet inclusion criteria for trials. Older adult patients who are enrolled in clinical trials tend to be healthier, with an Eastern Cooperative Oncology Group (ECOG) performance status (PS) of 0–1 (see Table 1 for ECOG PS definitions), making it difficult to apply the results of older adult women with breast cancer to the general population (Debled et al., 2011). Many providers may be unaware of open or ongoing clinical trials that are enrolling older adult patients (Kornblith et al., 2002). A study by Siminoff, Zhang, Colabianchi, Sturm, and Shen (2000) found that providers were significantly more likely to offer clinical trials to patients when they were aware of an open trial for which the patient was eligible. In addition, older adult patients may not want to participate in clinical trials because they may not be interested in aggressive treatment or may not want to feel like a test subject (Kornblith et al., 2002).

Providers rely on guidelines and recommendations to formulate the appropriate treatment for their patients. Evidence-based recommendations for older adult patients with MBC are limited because of the underrepresentation of this patient population in trials; therefore, providers do not have a strong basis from which to form opinions on appropriate therapeutic options for these patients (Biganzoli et al., 2012). In addition, many older adult patients do not receive optimal treatment for breast cancer because of therapeutic nihilism, both on the part of the treating provider and the patient (Raghavan & Suh, 2006). In essence, the provider and/or patient may feel that treatment may make little difference in extending an older adult patient’s life because of his or her advanced age, and that the benefit may not outweigh the potential side effects. Providers may underestimate a patient’s life expectancy, leading to ineffective or,

### TABLE 1. Eastern Cooperative Oncology Group Performance Status Definitions

<table>
<thead>
<tr>
<th>Score</th>
<th>Definition</th>
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<tr>
<td>0</td>
<td>Fully active; able to carry on all predisease performance without restriction</td>
</tr>
<tr>
<td>1</td>
<td>Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature (e.g., light housework, office work)</td>
</tr>
<tr>
<td>2</td>
<td>Ambulatory and capable of all self-care but unable to carry out any work activities; up and about more than 50% of waking hours</td>
</tr>
<tr>
<td>3</td>
<td>Capable of only limited self-care; confined to bed or chair more than 50% of waking hours</td>
</tr>
<tr>
<td>4</td>
<td>Completely disabled; cannot carry on any self-care; totally confined to bed or chair</td>
</tr>
<tr>
<td>5</td>
<td>Death</td>
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Treatment Recommendations

Studies that do report older adult data often are retrospective subgroup analyses, not large prospective trials (Biganzoli et al., 2012). Therefore, treatment often is based on extrapolation of study results from small analyses or from trials of younger adult patients (Biganzoli et al., 2012). The lack of clinical trial data in older women with breast cancer has limited the comprehensiveness of evidence-based treatment recommendations and guidelines (Biganzoli et al., 2012). However, recommendations for the management of older adult patients with breast cancer have begun to take shape. In 2007, the Société Internationale d’Oncologie Gériatrique (SIOG) published recommendations for the management of older adult patients with breast cancer (Wildiers et al., 2007). The recommendations were expanded in 2010 and updated in 2012 by a multidisciplinary task force created by SIOG and the European Society of Breast Cancer Specialists (Biganzoli et al., 2012). General recommendations provided by the task force were that all management decisions for older adult patients with breast cancer should consider physiologic (not chronologic) age, life expectancy, potential risks versus absolute benefits, treatment tolerance, patient preference, and potential barriers to treatment. With regard to chemotherapy for older adult patients with MBC, hormone therapy was recommended as the treatment of choice for those patients with estrogen receptor (ER)-positive MBC, whereas single-agent and combination chemotherapy were indicated for patients with ER-negative, hormone refractory, or rapidly progressing disease. The recommendations also stated that chemotherapy agents with more tolerable safety profiles, such as taxanes, capcitabine, and vinorelbine, were preferable in the management of older adult patients with MBC. In addition, the recommendations mentioned that, in older adult patients with MBC, bevacizumab has demonstrated a benefit with regard to progression-free survival (PFS); however, a limited overall survival (OS) benefit has been observed (Biganzoli et al., 2012; O’Shaughnessy et al., 2010). Although data are limited, human epidermal growth factor receptor 2 (HER2)-targeted therapies, such as trastuzumab and lapatinib, were found to be equally effective in older and younger adult patients with MBC (Biganzoli et al., 2012; Brunello et al., 2008; GlaxosmithKline, 2012). The SIOG and the European Society of Breast Cancer Specialists task force placed a strong emphasis on geriatric assessments, particularly the comprehensive geriatric assessment (CGA) (Biganzoli et al., 2012). The CGA is an individually tailored, multiple domain assessment that requires an interdisciplinary team of healthcare providers including oncologists, geriatricians, physical therapists, social workers, and nurses (Bernabei, Venturiero, Tarsitani, & Gambassi, 2000). Figure 1 shows the major domains of the CGA. Although implementation of the CGA is an ambitious task because of its extensive nature, the task force pointed out that strong evidence indicated that use of the CGA could improve survival, quality of life, tolerability, and compliance (Biganzoli et al., 2012). The overarching theme of the 2012 recommendations was that chronologic age should not be the only factor considered when managing the care of the older adult population. Instead, many factors need to be considered when treatment decisions are made for this population. Each patient should be evaluated individually by careful examination of functional status, cognitive status, comorbidities, nutritional status, treatment tolerance, and patient preferences, including beliefs and values. In addition, barriers to treatment should be identified, each patient should be carefully followed, and toxicities should be identified and appropriately managed.

Clinical Trials

From the review of several studies aimed at treating older adult patients with MBC, as well as older adult subanalyses of clinical trials, the evidence shows that many treatments which are effective in younger patients also are effective in this population.

Single-Agent Taxanes

Several phase II trials have assessed the activity of single-agent taxanes in the older adult population, including one post-hoc analysis of all three taxanes (Aapro, Tjulandin, Bhar, & Gradishar, 2011) (see Table 2). In 2005, a phase II study examined weekly paclitaxel as first-line treatment in 48 older adult patients with advanced breast cancer (Del Mastro et al., 2005). In that study, patients aged 70 years and older with stage III or IV breast cancer were treated with weekly paclitaxel 80 mg/m². The median age of patients was 74 years, and most patients had an ECOG PS of 0 or 1. For all patients, the median OS was 35.8 months. The most common comorbidities were hypertension (63%), arthritis (37%), and osteoporosis (29%). The overall response rate (ORR) for the 32 patients with stage IV disease was 44%. All patients were evaluable for safety. Of the AEs reported, most were grade 1 or 2, and the rate of each severe (grade 3 or
4) AE reported, including neutropenia, anemia, hypersensitivity reaction, fatigue, and neuropathy, was less than 10%. Severe cardiovascular complications did occur in the study, leading to death in two cases, and unacceptable toxicities within the first four cycles occurred in five other patients. A study by ten Tije et al. (2004) reported similar findings from another phase II study of weekly paclitaxel 80 mg/m² as first-line treatment for older adult patients with MBC. In that study, a dose increase to 90 mg/m² was allowed in the absence of unacceptable toxicity. The ten Tije et al. (2004) study enrolled 26 patients aged 70 years or older with stage IV hormone-refractory breast cancer. The median age of patients was 77 years, and most patients had a World Health Organization (WHO) PS of 0 or 1 (using the WHO scale, sensory and motor signs and symptoms are combined into one scale, rated from 0–4, with higher scores meaning worse neuropathy). The ORR in the 23 patients available for response assessment was 38%, and all were partial responses. In the 25 patients assessable for safety, most of the AEs reported were grade 1 and 2; however, grade 3 neutropenia and anemia occurred in 12% of patients. Grade 3 hypersensitivity reactions, fatigue, neuropathy, and vomiting each occurred in 4% of patients. The mentioned studies demonstrated that weekly paclitaxel was efficacious and had a tolerable safety profile in older adult patients with MBC.

Docetaxel also has been investigated in several phase II studies of older adult patients with MBC (D’hondt et al., 2004; Hainsworth et al., 2001). Hainsworth et al. (2001) treated 41 patients who were either older than aged 65 years or were considered to be poor candidates for combination therapy (i.e., comorbidities or poor tolerance for previous chemotherapy regimens). Docetaxel was given at a dose of 36 mg/m² weekly. Patients in that study ranged in age from 50–88 years, with a median age of 74 years; most patients had an ECOG PS of 0 or 1 and had visceral metastases. The ORR in the 36 patients available for response was 36%. All patients were assessable for safety, and the most common severe AEs were fatigue and asthenia (20%), diarrhea (10%), nausea and vomiting (7%), and peripheral edema (7%). Severe hematologic events were not common, with grade 3 or 4 anemia and leukopenia occurring in 4% and 5% of patients, respectively. D’hondt et al. (2004) performed a similar phase II study of docetaxel in 47 patients with MBC who were aged 70 years or older or ineligible for standard every-three-weeks docetaxel because of poor hematologic reserves, impaired liver function, intolerance to previous taxane therapy, or any combination of those reasons. Docetaxel was given at 36 mg/m² weekly. Patients ranged in age from 43–82 years, with a median age of 63 years, and most patients had a WHO PS of 1 or 2. Of the 37 patients evaluable for response, the ORR was 50%; of the patients for whom being aged 70 years or older was the only risk factor, the ORR was 40% (4 of the 10 evaluable patients had a partial response). In patients whose only risk factor was age (70 years or older, n = 11), one patient with hematologic abnormalities at baseline experienced grade 4 neutropenia, but no grade 3 AEs were reported. Grade 2 fluid retention and fatigue were reported in 18% of patients in this subgroup. The two studies demonstrated that docetaxel was effective and tolerable in older adult patients with MBC.

Beuselinck et al. (2010) compared weekly docetaxel and paclitaxel in a randomized phase II study of older adult or frail

<table>
<thead>
<tr>
<th>TABLE 2. Summary of Select Findings of an Analysis of Single-Agent nab-Paclitaxel Versus Paclitaxel and Docetaxel in Older Adult Patients With Metastatic Breast Cancer</th>
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<tbody>
<tr>
<td><strong>Efficacy Outcomes</strong></td>
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<tr>
<td></td>
</tr>
<tr>
<td>Paclitaxel 175 mg/m² (n = 32)</td>
</tr>
<tr>
<td>ORR (%)</td>
</tr>
<tr>
<td>Median PFS (Months)</td>
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<tr>
<td>Median OS (Months)</td>
</tr>
<tr>
<td>Grade 3 or 4 Adverse Effects</td>
</tr>
<tr>
<td>Neutropenia</td>
</tr>
<tr>
<td>Leukopenia</td>
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<tr>
<td>Neuropathy</td>
</tr>
<tr>
<td>Fatigue</td>
</tr>
<tr>
<td>Myalgia and arthralgia</td>
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ORR—overall response rate; OS—overall survival; PFS—progression-free survival

*Note.* Based on information from Aapro et al., 2011.
Clinical Journal of Oncology Nursing  •  Supplement to Volume 17, Number 1  •  Considerations for Older Adult Patients

Older adult patients often experience comorbidities, polypharmacy, and decreased organ function, which may affect their management and outcomes. However, healthcare providers should not use chronologic age as a factor when considering treatment options.

Clinical trials have demonstrated that many currently available chemotherapy options are efficacious and tolerable for older adult patients with metastatic breast cancer.

Nurses should take time to foster relationships with older adult patients to provide optimal care.

Combination Studies

Because of the potential toxicity and limited survival gain, few combination studies have been performed in this patient population (Biganzoli et al., 2012) (see Table 3). Hess et al. (2007) reported the results of a phase II trial of capecitabine plus vinorelbine as first-line treatment in older adult patients (aged 65 years or older) with MBC. In this study, vinorelbine was given at 20 mg/m² on days 1 and 8 of a three-week cycle and capecitabine was given at 1,000 or 1,250 mg/m² daily for two weeks in patients with or without bone involvement, respectively. The study enrolled 47 patients with bone involvement and 23 patients without bone involvement, with a median age of 72 and 75 years, respectively. Most patients in the trial had a WHO PS of 0 or 1. Patients with (n = 45) and without (n = 21) bone involvement who were assessable for response had ORRs of 45% and 57%, respectively. All patients were assessable for safety, and the most common grade 3 or 4 hematologic toxicity was neutropenia, occurring in six and eight patients with and without bone involvement, respectively. Only one grade 4

Exploration on the Go

ClinicalTrials.gov offers detailed information about ongoing national and international clinical trials for all cancer types. To access, open a barcode scanner on your smartphone, take a photo of the code, and your phone will link automatically. Or visit www.clinicaltrials.gov.
nonhematologic toxicity was reported—one case of nausea in a patient without bone involvement. Other key grade 3 nonhematologic AEs reported in patients with and without bone involvement were diarrhea (4% each) and anemia (2% versus 13%). Significant changes in quality-of-life scores (positive or negative) were not observed in either group. The authors concluded that the combination of vinorelbine and capecitabine was tolerable and effective and that the tolerability of the combination was evidenced by the low incidence of severe AEs and the fact that the quality-of-life indicators did not worsen.

Results from a phase II trial by Dong, Wang, Li, Cui, and Guo (2012) of gemcitabine in combination with vinorelbine in older adult patients with MBC were reported. In the study, gemcitabine was given at 1,000 mg/m² and vinorelbine was given at 25 mg/m² on days 1 and 8 of a three-week cycle. Fifty-one patients with a median age of 73 years were enrolled, and a majority of patients had an ECOG PS of 0 or 1. Most patients received the combination as first-line therapy (55%), but some received it as second line or greater (45%). Of the 48 evaluable patients, the response rate was 33%. At a median follow-up of 16.2 months, the median PFS and OS were 6.2 and 17 months, respectively. All patients were available for safety assessment, and the most common grade 3 and 4 AEs were leukopenia (27%), neutropenia (25%), anemia (14%), thrombocytopenia (10%), and fatigue (6%). The authors of the study suggested that gemcitabine plus vinorelbine was a viable alternative for the treatment of older adult patients with MBC after anthracycline and taxane therapy.

### Nursing Considerations

Education of older adult patients is a key factor in providing optimal care; therefore, nurses need to develop a trusting relationship with older adult patients. Allowing extra time for talking and listening will aid in the building of that trust. Many older adult patients have decreased cognitive abilities and may have difficulty understanding the information they are told. Some older adult patients may even be afraid or confused about their treatment. Slow and careful delivery and repetition of directions or information is an important way to aid in patient understanding and reduce anxiety. In addition, some older adult patients may find it difficult to accept change; therefore, incorporating and understanding a patient’s own personal beliefs and values may help to facilitate the learning process as well as aid in forming treatment regimens and management strategies. Important goals for healthcare providers when dealing with older adult patients are evaluating each patient as an individual and identifying optimal treatment strategies that balance life expectancy with treatment toxicity and quality of life. Healthcare providers should take as much time as is necessary to perform thorough examinations, which will aid in the identification and appropriate management of treatment-related toxicities in older adult patients. Older adult patients also are at risk for undertreatment of pain (Bernabei et al., 2000); one reason is that older adult patients are less likely to report pain symptoms than younger patients (Herr & Mobily, 1991). Therefore, assessment of pain using a rating tool such as a visual analog scale at every visit is important for ensuring that older adult patients are optimally treated. Treatment of MBC in the older adult is complicated and requires a multidisciplinary team approach.

Multiple members of a care team are required to manage the optimal physical, social, and psychological aspects of care. Because of that, nurses are a vital point of contact for patients, and they can help to gather and condense information from the individual areas of care, which may otherwise be too much for an older adult patient to take in. Well-informed patients will make decisions based on their own beliefs and values. Although those decisions may not always coincide with the nurse’s opinions, being a patient advocate and supporting patients’ decisions is a key role for nurses. The role of the nurse as a patient advocate also involves assisting the patient with communicating concerns to other healthcare providers. Ensuring that patients are well educated and building a trusting relationship will help patients to receive optimal care.

### Conclusion

Older adult patients with MBC often are quite different than the general population, with, among other things, increased comorbidities, polypharmacy, and decreased organ function (Biganzoli et al., 2012; Debled et al., 2011; McLean & Le Couteur, 2004). Therefore, adapting and applying knowledge from clinical trials of younger adult patients is not an optimal treatment strategy. With regard to the CGA, future work should focus on developing a more user-friendly assessment aimed at nurses that could be administered in the outpatient office setting—a setting that does not always offer enough time for a highly comprehensive assessment, such as the CGA. Although...
several trials and analyses have assessed the efficacy and safety of single-agent and combination chemotherapy, specifically in older adult patients with MBC, a need still exists for more trials examining treatment regimens, dosing, management strategies, tolerability, and outcomes in this patient population. A larger number of clinical trials in older adult patients with MBC will provide support for future recommendations and guidelines for the treatment of this population, which, in turn, will help to provide optimal treatment for older adult patients. Overall, formulation of a treatment plan for older adult patients should not only take into account age, but also multiple other factors including cognitive function, comorbidities, physical functioning, and beliefs. Finally, from the nursing perspective, taking time to nurture relationships with older adult patients will ultimately ensure that they receive the best care possible.

References


of oncologists’ perceptions of barriers to accrual of older patients
with breast carcinoma to clinical trials. Cancer, 95, 989–996.
doi:10.1002/cncr.10792
 clearance and an oxygen diffusion barrier hypothesis. Clinical
Pharmacokinetics, 34, 359–373.
Lickley, H.L. (1997). Primary breast cancer in the older adult. Can-
Manders, K., van de Poll-Franse, L.V., Creemers, G.J., Vreugdenhil,
G., van der Sangen, M.J.C., Nieuwenhuijzen, G.A.P., . . . Voogd,
breast cancer: A descriptive study according to age group.
BioMed Central Cancer, 6, 179.
Advances in Hematology and Oncology, 2, 457–465.
Miller, K. (2010). A meta-analysis of overall survival data from three
randomized trials of bevacizumab (BV) and first-line chemotherapy
as treatment for patients with metastatic breast cancer (MBC) [Ab-
www.asco.org/ASCOv2/Meetings/Abstracts?&vmview=abst_de-
tail_view&confID=74&abstractID=49471
Raghavan, D., & Suh, T. (2006). Cancer in the older adult popula-
tion: The protection racket. Journal of Clinical Oncology, 24,
1795–1796. doi:10.1200/JCO.2005.05.4502
aging: Impact on cancer management and decision making, part I.
Cancer Journal, 11, 499–460.
aging: Impact on cancer management and decision making, part II.
Siminoff, L.A., Zhang, A., Colobianchi, N., Sturm, C.M., & Shen, Q.
(2000). Factors that predict the referral of breast cancer patients
onto clinical trials by their surgeons and medical oncologists.
Journal of Clinical Oncology, 18, 1203–1211.
Smith, B.D., Smith, G.L., Hurria, A., Hortobagyi, G.N., & Buchholz,
Burdens upon an aging, changing nation. Journal of Clinical
Oncology, 27, 2758–2765. doi:10.1200/JCO.2008.20.8983
Tahir, M., Robinson, T., & Stotter, A. (2011). How not to neglect the
doi:10.1016/j.breast.2011.03.003
ten Tije, A.J., Smorenburg, C.H., Seynaeve, C., Sparreboom, A.,
paclitaxel as first-line chemotherapy for older adult patients
with metastatic breast cancer. A multicentre phase II trial. Eu-
.08.013
Wildiers, H., Kunkler, I., Biganzoli, L., Fracheboud, J., Vlastos,
G., Bernard-Mart, C., . . . International Society of Geriatric
individuals: Recommendations of the International Society of
Geriatric Oncology. Lancet Oncology, 8, 1101–1115. doi:10.1016/
S1470-2045(07)70378-9
opausal breast cancer patients aged 55 years and older. JAMA, 285,
885–892. doi:10.1001/jama.285.7.885
Zoli, M., Magalotti, D., Bianchi, G., Gueli, C., Orlandini, C., Grimal-
blood flow decrease in parallel with ageing. Age and Ageing,
28, 29–33. doi:10.1093/ageing/28.1.29