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# Breast Cancer in the Elderly

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## Abstract

Breast cancer is a serious health problem in the elderly female population. The approach to treating healthy women aged 65–70 years should be similar to treating younger patients with a similar stage and biological subtype of breast cancer. Greater individualization of treatment is necessary in the case of patients with worse parameters of functional efficiency and features of the frail syndrome. It should also be emphasized the need for closer cooperation with geriatricians, especially when defining the management plan and conducting systemic treatment in this group of patients. There is also a great need for research into the proper selection of treatment in elderly breast cancer patients. This is especially important in groups of patients with early and locally advanced breast cancer.

**Keywords:** breast cancer, elderly, frailty syndrome, comprehensive geriatric assessment

## 1. Introduction

Cancer is age-related. Increased life expectancy means that cancers in the elderly are becoming ever more common. More than three-quarters of cancer deaths are among those aged 65 years and older, and more than half among those aged 75 years and older [1].

This poses a challenge, especially for clinical oncologists, when choosing systemic therapy, due to the specificity of this group of patients. Unfortunately, the group of elderly patients is still underrepresented in clinical trials evaluating new cancer therapies. As a result, there is much less evidence-based information to guide proposed medical management.

Many publications emphasize that older patients are less likely to receive the most effective forms of systemic therapies. This can lead to poorer treatment outcomes and negatively affect patients' survival rates [2].

An important problem for the clinical oncologist is the comorbidities, which occur much more frequently in the elderly versus the younger population. Regrettably, comorbidities happen to be treated suboptimally, especially in people with no family support or care, which can cause additional problems complicating decisions about systemic therapy [3].

It should be pointed out that access to systemic therapy in the elderly population can be significantly hampered for social and economic reasons, especially for patients who live a considerable distance from oncological centers and find it difficult to come to regular visits. This factor is less important when it comes to other types of oncological therapies, namely surgery and radiation therapy, as both are not stretched over

time and, if necessary, a patient may be hospitalized until the completion of therapy. In the case of systemic therapy, patients need to visit the oncological center regularly (e.g. once a week or once a month), but they usually do not need to stay at the hospital for more than a few hours [4].

The primary risk factor for breast cancer is age. The median age of onset of this type of cancer is about 60 years. Over 40% of women with newly diagnosed breast cancer are 65 years and older. Since the population is clearly aging, the number of breast cancer patients may be expected to increase significantly in the coming years [1].

At present, the screening in most countries does not cover the population of 70 + – year-old women, mostly because this procedure is less cost-effective in comparison with the population of younger women. This is mainly due to the presence of concomitant diseases which reduce life expectancy, as well as the higher cost of treating breast cancer in elderly women. Besides, elder women are much less likely to report regularly for screening mammography. As a consequence, breast cancer detected in women at the age of 70 plus years is often at more advanced stages than in the case of younger women. According to some sources, over 40% of patients aged over 65 years are diagnosed with breast cancer only when distant metastases are already present [5].

Another very important problem in elderly breast cancer patients is systemic perioperative therapy. Although it is not a major problem to assess such patients eligible for endocrine therapy, a decision to assess a patient eligible for chemotherapy in many cases already raises many doubts among oncologists. The problem is even more compounded by the fact that older patients rarely consent to participate in clinical trials or they meet the exclusion criteria. As a result, elderly patients' therapy is suboptimal, usually not intensive enough, or they are sometimes assessed eligible for therapies that are too toxic for them; both options lead to a situation where the ultimate outcomes of treating older patients are worse.

The work published in 2011 by Smith et al. indicates that although the mortality rate from breast cancer in the <75-year-old population in the US declined by 2.5% per year from 1990 to 2007, breast cancer mortality in women aged 75+ years declined by only 1.1% per year [4]. In Europe, breast cancer mortality declined by 13% from 2000 to 2004 compared with the years 1990–1994; however, this decline was much more pronounced among women aged 35–64 years (17%) compared to only 6% for patients aged 65 years and older [5].

## **2. Factors affecting the choice of a course of action**

In most developed countries, 65 is the chronological age assumed to define the elderly. However, there is no doubt that this is a conventional limit, and the chronological age does not coincide with the biological one. Women aged 65 years are frequently individuals with no functional limitations under the conditions of most developed countries; nonetheless, in developing countries, this limit should be perhaps set much lower. The differences between communities can be very clear, e.g. for those born in 2011, the life expectancy is estimated at 48 to 82 years depending on the region of residence [6, 7].

Therefore, when assessing the eligibility for therapeutic management of an elderly breast cancer patient, not only do we need information about the biological features of breast cancer and its progress but also about comorbidities, received medications and most of all, the patient's biological age, as this information should crucially

determine further action to be taken. Most geriatric oncologists agree that the key element is to divide the elderly patients into those who are completely stable, with no co-existing medical conditions, i.e. so-called fit patients, and ailing patients with multiple co-existing internal diseases, i.e. frail patients. Thus, the suggested course of action should be based primarily on the patient's biological age.

Generally speaking, advanced age is associated with reduced tolerance to physiological stress, more frequent occurrence of comorbidities, more intense cognitive disorders, and decreased social support. A patient over the age of 70 years can be expected to suffer on average from three comorbidities. It has been shown that most comorbidities such as renal failure, liver failure, and cerebrovascular disease are mostly associated with an increased risk of death from causes other than breast cancer. The occurrence of any serious and chronic comorbidities is assumed to play a major role in determining the predicted survival time in older patients aged 50–79 years and diagnosed with breast cancer.

This is to some extent confirmed by the study results published in 2011 by Schonberg et al. This study evaluates mortality from the cause of death in 66,000 women aged over 67 years after a breast cancer diagnosis compared to a properly selected group of women without breast cancer [8]. Women with ductal carcinoma in situ (DCIS) or stage I invasive breast cancer had a lower risk of death than the controls, and the most common cause of death was cardiovascular disease. Patients with a diagnosed stage II breast cancer had greater mortality than controls but among women aged 80 years and older, cardiovascular disease was still the prevailing cause of death. In contrast, for stage III or IV breast cancer, breast cancer itself was the commonest cause of death, even with the oldest patients.

Undoubtedly, the biggest decision-making problem is the eligibility assessment or the decision to abandon perioperative chemotherapy.

It seems that the most significant factor to take into account when making that decision should be an assessment of the patient's functional status, which is defined as an individual's ability to perform normal daily activities. In their work, Braithwaite et al. studied a cohort of 2200 women with breast cancer who received adjuvant therapy. Functional limitations in this group were associated with older chronological age, lower education level, and obesity. It has been shown that during the median follow-up of 9 years in patients with functional limitations, the risk of death increased from all causes but not from breast cancer (HR 0.90; 95% CI 1.03–1.92) [9].

Ideally, all elderly patients with indications for perioperative chemotherapy according to the generally applicable guidelines should have a comprehensive geriatric assessment (CGA) or at least a functional status assessment, which, unfortunately, is not possible in most cancers, mainly due to lack of time and qualified medical staff [10].

### **3. Screening procedures**

For over 30 years, the main determinants of improved survival rates for cancer patients have been considered early detection of the disease, i.e. the screening tests that make this possible (namely screening mammography) and the introduction of adjuvant therapy. Most randomized studies evaluating the value of mammography screening did not include women aged 75 years or older. Therefore, the epidemiological benefits of screening in this age group are unknown. Observation studies suggest that older women with a life expectancy of 10 years plus should be taken into account

in screening tests. The breast cancer mortality is estimated to be reduced by about 0.2% if active mammography screening is extended beyond the age of 70 years. However, in each case, a decision to continue mammography screening in 70 + – year-old women should be made on a case-by-case basis unless other guidelines are developed [11].

#### **4. Breast cancer biology in elderly patients**

Most available publications report that breast cancer in older women is less aggressive. In this group, hormone-dependent cancers are diagnosed more frequently, and overexpression of the HER2 receptor, grade 3 cancers, and high Ki67 values are less common.

The odds of developing triple-negative cancer in women aged <40 years are 1.53 times higher than in patients aged over 60 years, but 15–18% of older patients are diagnosed with this breast cancer subtype, which confers a poor prognosis [12].

Age does not significantly affect the cancer's histological subtype, but lobular, mucinous, and papillary carcinomas are slightly more common in older patients. For example, mucinous carcinomas account for 4–6% of cancers diagnosed over the age of 75 years, whereas only 1% of premenopausal women are diagnosed with this type of cancer [12, 13].

#### **5. Distinctions in the management of systemic therapy in elderly patients**

When conducting oncological systemic therapy in the geriatric population, various side effects may be observed that are directly related to the type of therapy. Depending on the formation mechanism, they may occur with similar or greater frequency than in younger age groups.

However, when treating the elderly, we also encounter problems that are not at all or very rarely described in younger patients. They mainly concern the aging physiology as well as the psychological and sociological levels [14, 15].

The biology of some cancers and their response to therapy changes as the patient ages. In addition, physiological changes associated with aging can affect the tolerance of the drugs. The lower renal and hepatic performance, as well as low bone marrow reserve, which arises from the physiological changes in the aging body, can fundamentally affect the pharmacokinetics and pharmacodynamics of the drugs.

Comorbidities, mainly cardiovascular and nervous ones, are also much more common in elderly patients. Some of those patients may be malnourished and experience geriatric syndromes such as incontinence, tendency to fall, balance disorders, frailty syndrome, and dementia. In addition, in this group of patients, we often deal with polypragmasy [3, 12, 14].

All of these factors can significantly complicate or even prevent optimal systemic therapy. Furthermore, if patients face other types of medical problems, these can significantly define their life expectancy and considerably impair their quality of life [16]. What is of particular importance is the detection of frailty syndrome. Literature data indicate that over half of elderly oncological patients exhibit some or all features of frailty syndrome. This group of patients specifically is often at increased risk of mortality, postoperative complications, and serious side effects associated with systemic therapy, especially chemotherapy [15, 17].

Psychosocial factors have been described as having a significant impact on therapeutic decisions and the course of treatment. Elderly patients living alone or with a person of a similar age are less likely to accept possible problems that may arise during treatment.

Similar difficulties may arise for people having difficult access to transportation and those residing in nursing homes. In many countries, governmental or nongovernmental initiatives are emerging to reduce barriers to access oncological treatment among the elderly and disabled. These may involve medical staff visiting the patient at their home to inject or infuse drugs, blood draws for laboratory tests, etc., as well as telephone monitoring of the patient's condition to detect possible adverse symptoms in advance.

Patients with dementia pose a significant problem for oncologists. In most clinical situations, people with minor dementia can understand the rules of the suggested therapy and make proper decisions on their own, if given enough time to explain them properly. In the case of people with more advanced dementia, the caregiver must participate in the decision-making process concerning the therapy and further care provided to the patient.

It should also be pointed out that older patients may prefer therapies that have the potential to improve their quality of life, whereas longer survival may be of lower importance for them. The Silvestri study, for example, assessed the preferences for chemotherapy in patients with advanced lung cancer. Only 22% of patients chose chemotherapy for 3 months' improvement in survival, but the majority (68%) would choose chemotherapy if it substantially reduced symptoms without prolonging life [18].

## **6. Individual approach to systemic therapy in elderly patients**

As the dependencies between genetic and environmental factors in the aging process are quite complex, the aging process for each person is slightly different. Therefore, the chronological age alone does not reflect a patient's condition, nor can it be considered a predictor of response to treatment and the occurrence of side effects or other therapy-related problems. To be able to make optimal decisions about systemic therapy in elderly patients, you need to characterize the functional reserve, both from the physical and mental point of view, as well as assess the number and severity of comorbidities and evaluate the patient's social capabilities [17, 19].

It is also important to make certain modifications, if any, to the treatment of comorbidities, that includes consultations with other specialists, especially in the field of geriatrics, but also rehabilitation, nutrition, etc.

During systemic therapy, it is important to implement any methods that can reduce side effects.

The most important element that is fundamentally responsible for the success of systemic therapy in a group of geriatric patients seems to be the individual assessment of the patient's condition before deciding on their eligibility for therapy. This assessment should be done as early as the initial visit to the clinical oncologist [20, 21].

At present, we have several tools that can help us assess the risk of serious complications arising during systemic therapy. The most commonly recommended tools are the CRASH score and CARG score.

Extermann developed the CRASH score calculator (<https://moffitt.org/eforms/crashscoreform>), which can be used to assess the risk of serious chemotherapy

complications among elderly patients based on information about the planned therapy and patient characteristics. The main elements indicating the risk of hematologic toxicities are the instrumental activities of daily living score (IADL), blood lactate dehydrogenase level, diastolic blood pressure value, and estimated toxicity of the chemotherapy regimen. In contrast, the incidence of serious non-hematological complications is supported by the patient's ECOG score, cognitive status using the mini-mental state examination (MMSE) score, nutritional status using the mini-nutritional assessment (MNA) score, and the toxicity of the therapy regimen [22].

Huria was the author of a similar tool, namely the CARG score calculator ([https://www.mycarg.org/?page\\_id=934](https://www.mycarg.org/?page_id=934) or <https://www.evidencio.com/models/show/520>), which can be used to assess the risk of serious complications of systemic therapy based on such information as the patient's condition (age, the number of falls they have had within the past 6 months, limited social activity, and need for assistance with medications), laboratory test results (creatinine and hemoglobin levels), and the proposed therapy regimen. In addition, Huria emphasized that the Karnofsky Performance Status (KPS) commonly used by oncologists to assess the performance status of the elderly is not useful at all [23].

Recently, we have observed some opinions that point out the importance of optimizing psychosocial and physical health before starting systemic therapy in older patients. This involves the identification of patient's needs in this regard. The International Society of Geriatric Oncology (SIOG), an organization dedicated to addressing oncology issues in the elderly, recommends conducting a comprehensive geriatric assessment (CGA) before undertaking any planned surgical intervention or systemic therapy in elderly oncological patients. The value of this assessment lies not only in determining the risk of possible complications but primarily in seeing it as a possibility of optimization and individualization of treatment [3, 19].

Kalsi published the results of a randomized trial involving 135 cancer patients over the age of 70 years who were eligible for chemotherapy. The observational control group (70 patients) received standard oncological therapy, while the intervention group (65 patients) underwent risk stratification using a patient-completed screening questionnaire; subjects were assigned to appropriate groups, depending on the risk of complications. Those at high risk of complications had a comprehensive geriatric assessment performed and, based on the results, were given plans for appropriate multidisciplinary interventions. It turned out that patients in the intervention group were more likely to follow the expected treatment plan and were less likely to require any modification of therapy [10, 24].

Thus, there seems to be a need to change the approach to oncological therapy of elderly patients taking into account the need to implement measures currently referred to as prehabilitation [25].

## **7. Surgery and radiotherapy for breast cancer**

Unquestionably, unless there are very significant contraindications to anesthesia, stage II, post-neoadjuvant therapy breast cancer patients (and in selected cases stage III patients that have not received neoadjuvant therapy) should be offered surgical therapy, which may involve breast-conserving surgery or mastectomy.

In selected cases, i.e. in patients with a predicted survival time shorter than 5 years, axillary procedures as well as any surgical treatment in general may be abandoned when the preinvasive form of breast cancer has been diagnosed.

However, studies have shown that surgical treatment is often abandoned in elderly patients for various reasons. The study of Bastiaannet et al., which involved more than 120,000 women, showed that older age was associated with a lower percentage of surgeries. Whereas more than 93% of women under 80 years of age underwent surgery, the percentages of radical breast cancer surgery performed in the 80–84, 85–89, and over 90 years of age groups totaled, 83%, 65%, and 41%, respectively. Also, it has been shown that older patients were less often eligible for radiation therapy after breast-conserving surgeries. In that group, in women under the age of 75 years, radiotherapy was used in more than 90% of cases, while in the age groups of 75–79, 80–84, 85–89, and 90+ years, it totaled 86%, 71%, 36%, and 15%, respectively. However, this study does not report on how the decision of radiotherapy was dependent on cancer recurrence risk factors. The same paper claims that the eligibility for hormone therapy (without surgical treatment) rate increased with age. It ranged from <1% in patients below the age of 65 years up to 47% in patients aged 90 years and older [26].

Another study attempted to answer the question of whether the lower number of surgeries performed arose from the functional status or biological age of patients with stage I, II, or III breast cancer. Multivariate analysis showed that women aged 85 years and older were significantly less likely to undergo breast cancer surgery having taken into account the patient's possible negative attitude toward the procedure and their functional status (the odds ratio [OR]: 0.18, 95% CI 0.07–0.44). These data suggest that objective considerations are not always decisive when assessing older patients' eligibility for surgery [27].

Most patients without functional status limitations should be eligible for adjuvant radiotherapy following breast-conservative surgery. However, it should be noted that even during the visit to discuss surgical treatment options with the patient, they should be informed of the radiation therapy options, as some patients may decide not to have radiation therapy for the fear of its consequences or for social reasons [28].

## **8. Systemic perioperative therapy**

Older patients with early forms of breast cancer and perfect or very good functional status may be offered adjuvant therapy per standard treatment guidelines for younger patients. In the case of patients with multiple internal concomitant diseases, cognitive disorders, and functional status limitations, the suggested therapy should mainly depend on the feasibility and expediency of surgical therapy. If surgery had been performed, in most patients with an estimated survival time of up to 5 years, systemic therapy and radiotherapy may be abandoned. On the other hand, those patients that do not agree to surgery or who cannot have surgery due to medical contraindications should receive hormone therapy (in case of hormone-sensitive cancers) or remain under the supervision of an oncologist or a general practitioner (GP).

It is believed at present, that breast cancer patients aged 65–70 years should be initially evaluated in terms of their general condition and internal diseases by an oncologist, and only the preselected patients should undergo geriatric screening tests (mainly to evaluate their functional status). To this end, it is recommended to use the G8, VES-13, TRST 1+ scales, or Groningen Frailty Index. This evaluation should be also performed for all older patients. In the case of some patients, the next necessary step before making any decisions about the therapy may be a comprehensive geriatric evaluation and geriatric consultation [29–31].



This will help to select a group of older patients who should be eligible for or totally excluded from chemotherapy. Additionally, the International Society of Geriatric Oncology (SIOG) guidelines suggest the need for serial evaluation of functional status during adjuvant therapy to identify deterioration of the patient's health and undertake necessary intervention as early as possible [24, 32].

### 8.1 Fit patients

The treatment management of fit older breast cancer patients is identical to that of younger women and depends primarily on the evaluation of the recurrence risk factors. As a general rule, some patients should be offered neoadjuvant therapy.

The preferred cytostatic agents for perioperative treatment in this group of patients are anthracyclines and taxanes. However, you should remember the risk of myocardial damage after anthracyclines; therefore, women with significant cardiac comorbidities should be excluded from therapy with this group of cytostatic agents.

The study conducted by Pinder et al., which included 44,338 women aged 66–80 years with stage I–III breast cancer with no history of heart failure, showed that with a follow-up median of 56 months, evidence of heart failure after 5 and 10 years after the end of treatment in the group of patients who received anthracyclines (4000 patients) totaled 19% and 38%, whereas in the case of patients that did not receive anthracyclines, they totaled 18% and 33%, respectively. In the case of patients who did not receive any chemotherapy, it totaled 15% and 29%. Heart failure symptoms were observed more frequently in Black patients, as well as in patients with hypertension, diabetes, and coronary artery disease [33].

Other options involving slightly less cardiotoxicity are epirubicin or liposomal anthracyclines.

In patients who cannot receive anthracyclines, a TC (docetaxel with cyclophosphamide) regimen can be used. In a randomized phase III clinical trial published in 2009, four cycles of TC were shown to produce superior median progression-free survival and median overall survival compared with four cycles of AC, in patients with stage I–III cancer aged 65 years and older [34].

Another option is a CMF regimen (cyclophosphamide, methotrexate, 5-fluorouracil), but this is not the preferred option due to the high risk of hematological complications in elderly patients [35].

Where we are dealing with patients with lower performance status or significant internal comorbidities, a reasonable option may be paclitaxel administered weekly for 12 weeks at a dose of 60–80 mg/m<sup>2</sup> [36].

Single-agent capecitabine is not recommended as adjuvant therapy in elderly patients. A randomized phase III trial involving 633 patients aged 65 years and older with early-stage breast cancer, which was published in 2009, showed that capecitabine produced worse therapy results. During the follow-up (a follow-up median of 2.4 years), a progression-free survival rate totaled 68% versus 85%, whereas an overall survival rate was 85% versus 91% after a follow-up median of 3 years [37].

Adjuvant therapy combined with trastuzumab and taxanes is recommended for breast cancer patients with overexpression of HER2. Sequencing of anthracyclines is usually not recommended due to the increased risk of heart failure.

Data on the use of docetaxel and carboplatin in combination with trastuzumab, as well as with trastuzumab and pertuzumab, are very limited in women aged 70 years and older. Rather, a TC (docetaxel with cyclophosphamide) regimen should be

considered in selected cases in patients with no functional status limitations and higher-stage cancers.

Also, in the case of HER2-positive cancer patients, chemotherapy can be often limited to paclitaxel administered weekly for 12 weeks. In contrast, for patients diagnosed with stage I and II hormone-sensitive, HER2-positive cancer, hormone therapy in combination with trastuzumab may be a sufficient treatment option [37, 38].

For patients with cardiovascular comorbidities, consideration may be given to shortening the length of trastuzumab therapy, as trastuzumab-induced cardiotoxicity is linked to the length of exposure [38, 39].

Until now, there are no guidelines pertaining to the group of older patients regarding prolonged anti-HER2 cancer therapy with neratinib, nor the use of trastuzumab emtansine for the minimal residual disease after the completion of neoadjuvant therapy.

Preoperative hormone therapy is recommended for patients with hormone-sensitive cancers at a locally advanced stage, or for those interested in conserving therapy but whose anatomical conditions prevent it at the time of breast cancer diagnosis. The recommended group of drugs in this case is aromatase inhibitors. They should be administered for 6–9 months and, of course, should be continued after the surgery, as long as the response to therapy is observed [40].

Adjuvant hormonal treatment should be offered to all patients with hormone-sensitive breast cancer, regardless of age. Aromatase inhibitors are preferred in older women due to the greater benefit of such treatment in this patient group versus tamoxifen and a more favorable safety profile. However, for patients at high risk of cardiovascular complications and with advanced osteoporosis or aromatase inhibitor intolerance, tamoxifen is also a reasonable option.

The optimal duration of adjuvant hormone therapy is not fully established. The minimum therapy duration should be 5 years, but in selected patients, it may be recommended to extend the therapy up to 10 years [41, 42].

## **8.2 Patients with evidence of frailty syndrome**

Patients with evidence of a frailty syndrome, short life expectancy, and those wishing to avoid any therapy-related toxicities should be treated on a case-to-case basis [43, 44].

In some patients, systemic therapy can simply be abandoned (except for hormone therapy in hormone-sensitive cancer patients).

Also, in this group, aromatase inhibitors as hormonal therapy are preferred, but there are no results of prospective studies in this patient population comparing the efficacy and safety of tamoxifen versus aromatase inhibitors.

Similarly, no results of randomized trials comparing more aggressive treatments with hormone therapy, or hormone therapy only, have been published.

## **8.3 Metastatic breast cancer**

Metastatic breast cancer remains incurable regardless of the patient's age, and any available therapy is palliative. Only about 20% of metastatic patients survive 5 years.

However, even in older patients with metastases, there is a high risk of death from causes other than breast cancer [8, 12].

The goal of therapy in metastatic patients is to maintain the highest quality of life for as long as possible.

## 8.4 Triple-negative cancer

The general approach to treating older patients with metastatic triple-negative breast cancer is similar to that followed in younger patients; it consists of using single agents sequentially, except for patients with rapidly progressive symptomatic metastases [45].

Radiation therapy should be considered for older patients with symptomatic brain and bone metastases.

Older age has been proven to be a risk factor for early death in those who present with de novo metastatic triple-negative breast cancer.

In a group of older patients, several single agents are recommended as preferred single agents. These include capecitabine, weekly paclitaxel, nab-paclitaxel, eribulin (as second- and third-line treatment), liposomal doxorubicin, vinorelbine, and gemcitabine [34, 45, 46].

The choice of drug should be based on the toxicity profile. As first-line therapy, response rates vary greatly according to patient characteristics, and average about 30–50%, while progression-free survival time averages about 3 to 6 months. Second- and third-line therapies are less effective.

In comparison with younger age groups, the use of chemotherapy in patients aged 80 years and older has been shown to be associated with a significantly higher rate of hospitalizations (32%), red blood cell concentrates transfusions (18%), and reduced doses of cytostatic drugs, skipping and/or delaying subsequent doses (68%) [47, 48].

Other drugs that can be considered for the treatment of elderly patients include olaparib (poly(ADP-ribose) polymerase inhibitor). However, as with most trials of newer agents, the registration study of that drug in breast cancer patients involved only 15 patients aged 65 years and older [34, 49].

Modulating the immune system using checkpoint inhibitors also shows promise, but almost no data are available from randomized clinical trials in older breast cancer patients [50].

## 8.5 Hormone-dependent cancer

The primary treatment option for generalized hormone-dependent breast cancer is hormone therapy. Preferred options for first-line therapy are aromatase inhibitors or fulvestrant. In most cases, hormone therapy may be combined with cyclin-dependent kinase 4/6 inhibitors. A particular agent from this group should be selected depending on the expected side effects. Most authors suggest that palbociclib may be the agent best tolerated by elderly patients [51, 52].

The second-line therapy should include a hormonal drug that has not been used yet in combination with a CDK 4/6 inhibitor (provided it has not been used before). The combination of hormone therapy with alpelisib is also recommended in older patients with PIK3CA mutations [53].

In the case of patients with hormone resistance, chemotherapy is also an option, according to standard guidelines for patients with triple-negative cancers.

## 8.6 Cancer with overexpression of the HER2 receptor

For older patients with HER2-positive cancers, pertuzumab, trastuzumab, and a taxane are recommended as first-line therapy options, similarly to younger age groups, whereas paclitaxel is the preferred option in this case [37, 49].

Patients with poorer functional status may be considered for pertuzumab and trastuzumab in combination with cyclophosphamide administered orally at a dose of 50 mg/day [54].

The combination of dual anti-HER2 blockade with an aromatase inhibitor is also a recommended option in patients with HER2-positive hormone-sensitive cancers.

In the next line of therapy, trastuzumab emtansine (T-DM1) is recommended due to the good safety profile of this drug in the elderly patient population.

For patients with good functional status, other drugs that act on the HER2 receptor may be considered, but information on the safety of these drugs in the group of patients older than 65 years is very limited [47, 49].

### **8.7 Patients with evidence of frailty syndrome**

Patients with generalized breast cancer and evidence of frailty syndrome, significant cognitive disorders, or multiple co-existing internal diseases should be treated on a case-to-case basis. It should be noted that the proposed treatment must not cause more problems for the patient and her family than the cancer itself. Therefore, sometimes the best option may be to use symptomatic therapy only in hospice-palliative care [55].

## **9. Conclusion**

Breast cancer is a serious health problem in the elderly female population. The approach to treating healthy women aged 65–70 years should be similar to treating younger patients with a similar stage and biological subtype of breast cancer.

Greater individualization of treatment is necessary for patients with worse functional status and evidence of frailty syndrome. The need for closer cooperation with geriatricians should be also pointed out, especially when determining the management plan and conducting systemic therapy in this group of patients.

There is also a great need for research on the appropriate choice of therapy for elderly breast cancer patients. This is of particular importance in early and locally advanced breast cancer patients.

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