## E22. Breast cancer in the elderly

M. Aapro\*

Multidisciplinary Oncology Institute, Genolier, Switzerland

We have recently reviewed the treatment of elderly, in particular frail, women with breast cancer. 1 This presentation at the 7th European Breast Cancer Conference will focus on some of the suggested solutions for these issues specific to elderly patients. A reduction in breast cancer mortality in women aged 70 years or more has only been reported in some European countries. 2 Retrospective analyses have demonstrated that inadequate treatment on the basis of age alone is not rare.<sup>3</sup> Risk of relapse and death from breast carcinoma, toxicity of anticancer treatments and life expectancy are key elements when adjuvant treatment choices are discussed. 4 A geriatric assessment is suggested as the best means to categorise patients and to uncover potential correctable or non correctable limitations. 5 An analysis of five randomised studies <sup>6</sup> fails to show significant detriment on survival in patients who only have tamoxifen treatment, but omitting surgery leads to an unacceptably high proportion of local relapses. Sub-analyses demonstrate that advanced age does not decrease the adjuvant activity of aromatase inhibitors. 7 Provided due care is taken, there is limited potential for worsening preexisting osteopaenia/ osteoporosis. 8 The randomised adjuvant study of CMF (cyclophosphamide, methotrexate, 5-fluorouracil) or AC (doxorubicin, cyclophosphamide) versus capecitabine clearly indicates that age is not a limiting factor for benefit of standard chemotherapy in fit elderly women in oestrogen receptor-negative cases. 9 There is, however, evidence that CMF is less active and induces non negligible toxicities in elderly women 10 while taxanes can be used in fit elderly. 11 Trastuzumab roughly abates relapses of HER-2 positive disease by 40% independently from age and other relevant prognostic factors. 12 Older breast cancer patients relapsing during or after adjuvant treatment with tamoxifen can be treated with aromatase inhibitors, which have been demonstrated to be superior to tamoxifen in terms of response rate and progressionfree survival. 13 Fulvestrant's safety and activity in elderly patients is poorly documented but there is no reason not to use this agent. As a general principle, elderly patients with metastatic breast cancer are expected to derive similar benefits from chemotherapy compared to their younger counterparts in terms of response and delay of progression, but since the risk of toxicity is increased, their quality of life may be impaired during chemotherapy administration. 14 Heterogeneous age limits and entry criteria, low patient numbers, patient selection bias, different endpoints (radiological response, delay of progression, quality of life) and even early interruption are all factors hampering an objective comparison of results. We consider monotherapy as the most reasonable choice because compliance of unfit patients and ability to treat toxicities at home may be limited and therefore the risk of serious adverse events and inadequate dose intensity with polychemotherapy surpasses the potential gain in efficacy. 14,15 Weekly paclitaxel is not the first choice in the presence of diabetes or peripheral neuropathy, capecitabine and methotrexate doses should be adjusted in case of reduced renal function, and standard anthracyclines should be avoided in women with cardiovascular risk factors. Oral drugs such as capecitabine, vinorelbine and metronomic cyclophosphamide plus methotrexate may appear attractive for elderly patients, but several problems such as correct intake of prescribed dose, interference with food or concomitant medications (i.e. capecitabine with warfarin), self-reduction or escalation of dose, inadequate storage, etc. may all interfere with the ultimate efficacy of the treatment. More studies should address this population in the near future in order to develop models of prognostic stratification of patients allowing also the prediction of different toxicity rates according to pre-treatment levels of functional autonomy and comorbidity. 14,16 Standardised tools of assessment are needed and one should give the greatest attention to quality of life and to preservation of functional autonomy rather than to the classic endpoint of tumour response, because these are the most relevant outcome measures for most elderly patients.

## **Conflict of interest statement**

None declared.

## References

- Aapro M, Monfardini S, Jirillo A, Basso U. Management of primary and advanced breast cancer in older unfit patients (medical treatment). *Cancer Treat Rev* 2009; 35:503–8.
- [2] Héry C, Ferlay J, Boniol M, Autier P. Changes in breast cancer incidence and mortality in middle-aged and elderly women in 28 countries with Caucasian majority populations. *Ann Oncol* 2008;19:1009–18.
- [3] Bouchardy C, Rapiti E, Gerald F, et al. Undertreatment strongly decreases prognosis of breast cancer in elderly women. J Clin Oncol 2000; 21: 3580–87.

- [4] Muss HB, Biganzoli L, Sargent DJ, Aapro M. Adjuvant therapy in the elderly: making the right decision. *J Clin Oncol* 2007;25: 1870–5.
- [5] Exterman M, Meyer J, McGinnis M, et al. A comprehensive geriatric intervention detects multiple problems in older breast cancer patients. Crit Rev Oncol Hematol 2004;49:69–75.
- [6] Hind D, Wyld L, Beverley CB, Reed MW. Surgery versus primary endocrine therapy for operable primary breast cancer in elderly women (70 years plus). *Cochrane Database Syst Rev* 2006;(1): CD004272.
- [7] Crivellari D, Sun Z, Coates AS, et al. Letrozole compared with tamoxifen for elderly patients with endocrine-responsive early breast cancer: the BIG 1-98 trial. *J Clin Oncol* 2008;26:1972–9.
- [8] Hadji P, Body JJ, Aapro MS, et al. Practical guidance for the management of aromatase inhibitor-associated bone loss. *Ann Oncol* 2008;19:1407–16.
- [9] Muss HB, Berry DA, Cirrincione CT, et al. Adjuvant chemotherapy in older women with early-stage breast cancer. N Engl J Med 2009; 360:2055–65.
- [10] Crivellari D, Bonetti M, Castiglione-Gertsch M, et al Burdens and benefits of adjuvant cyclophosphamide, methotrexate, and fluorouracil and tamoxifen for elderly patients with breast cancer: the International Breast Cancer Study Group Trial VII. *J Clin Oncol* 2000; 18:1412–22.

- [11] Loibl S, von Minckwitz G, Harbeck N, et al. Clinical feasibility of (neo)adjuvant taxane-based chemotherapy in older patients: analysis of >4,500 patients from four German randomized breast cancer trials. *Breast Cancer Res* 2008;10(5):R77.
- [12] Dahabreh IJ, Linardou H, Siannis F, Fountzilas G, Murray S. Trastuzumab in the adjuvant treatment of early-stage breast cancer: a systematic review and meta-analysis of randomized controlled trials. *Oncologist* 2008;13:620–30.
- [13] Biganzoli L, Licitra S, Claudino W, Pestrin M, Di Leo A. Clinical decision making in breast cancer: TAM and aromatase inhibitors for older patients – a jungle? Eur J Cancer 2007; 43: 2270–8.
- [14] Wildiers H, Kunkler I, Biganzoli L, et al. Management of breast cancer in elderly individuals: recommendations of the International Society of Geriatric Oncology. *Lancet Oncol* 2007;8:1101–15.
- [15] Cardoso F, Bedard PL, Winer EP, et al. International guidelines for management of metastatic breast cancer: combination vs sequential single-agent chemotherapy. J Natl Cancer Inst 2009;101:1174–81.
- [16] Aapro MS, Köhne CH, Cohen HJ, Extermann M. Never too old? Age should not be a barrier to enrollment in cancer clinical trials. *Oncologist* 2005;10:198–204.