# Medical oncology

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Age-associated conditions may limit cancer chemotherapy administration in elderly cancer patients with advanced chemosensitive neoplasia: the most frequent tumour types observed by medical oncologists and requiring chemotherapy with the possibility of achieving useful objective responses are breast cancer, lung cancer, non-Hodgkin's lymphomas, colorectal carcinoma, ovarian carcinoma and bladder carcinoma. Also, in operable breast and colon carcinomas, where there is an established indication for adjuvant chemotherapy, there is uncertainty on the need for active treatment in elderly cancer patients.

The available information on the neoplasia most frequently requiring chemotherapy in the advanced and adjuvant setting for older patients will be examined here.

## Breast cancer

*Advanced breast cancer*

Older postmenopausal women appear to have a better response and overall survival when treated with tamoxifen, since oestrogen receptor (ER)-positivity is higher. Toxicity of tamoxifen is low. In the absence of life-threatening disease progression, tamoxifen should be the initial option followed by aromatase inhibitors or progestins at progression. Still 20% of patients with negative receptor status respond to tamoxifen. When all hormonal options have been exhausted, elderly women should be treated with chemotherapy. The anthracyclines are the most effective agents, but cardiac toxicity is more common in the elderly [1]. Because of the association with low cardiac toxicity, liposomal doxorubicin should receive further attention. Use of desrazoxane to decrease the cardiotoxicity of anthracyclines should be considered. Bone marrow depression is more frequent in elderly cancer patients, but attempts at a dose reduction for cyclophosphamide, methotrexate, 5-fluorouracil (CMF) treatment have resulted in a lower response rate [2].

At this time, no specific combination chemotherapy regimens have been tested in elderly woman. CMF, CNF (Cyclophosphamide, Novantrone and 5-fluorouracil) or other anthracycline-including combinations, can be considered in non-fragile patients possibly with the use of granulocyte-colony stimulating factor (G-CSF), while in fragile patients single agent chemotherapy should be preferred. The most interesting compound used alone is vinorelbine [3], while the docetaxel or paclitaxel weekly schedules of administration show promise for the future.

*Adjuvant therapy*

Whether adjuvant chemotherapy should be used to treat breast cancer in elderly patients over 70 years of age is still matter of controversy [5].

There is a general agreement that tamoxifen adjuvant therapy should be administrated to any woman with an invasive breast cancer $>1$ cm [4]. The net benefit that one can expect from the addition of chemotherapy to tamoxifen may be very little. However, no trial addressing this question has been specifically conducted in women older than 70 years of age. Decision-making should then take into account for the selection of possible treatment of patients with chemotherapy adverse prognostic factors (e.g. $>3$ lymph-nodes), age-associated conditions (with the help of the multidimensional geriatric evaluation) and type of chemotherapy. Probably CMF should still be the preferred standard.

## Lung cancer

*Non-small cell lung cancer (NSCLC)*

Many of the newer platinum-based combination chemotherapy regimens carry the risk of significant toxicity in elderly cancer patients. Development of modern anti-emetics and the availability of G-CSF may allow the use of these regimens also in non-fragile patients. A reasonable alternative can

be single agent chemotherapy with vinorelbine to achieve responses and improve quality of life without significant toxicity [6]. Vinorelbine can be definitely suggested for fragile patients.

*Small cell lung cancer (SCLC)*

Single agent chemotherapy with VP-16 or with teniposide has been suggested for elderly patients with advanced SCLC, but the combination of VP-16 and cisplatin is probably superior [7] and should be applied in non-fragile patients. Radiation therapy in the case of limited disease located in the left lung may carry the risk of cardiac effects in the elderly with SCLC. The side-effects of cranial irradiation have never been properly evaluated in elderly (e.g. with a minimal status evaluation), but should be considered in patients with a better prognosis, before planning a prophylactic cranial irradiation.

## Non-Hodgkin's lymphomas (NHL)

Advanced age is an adverse prognostic factor for aggressive NHL [8].

Elderly patients have a lower rate of durable complete response (CR) and survival than other adults. Up to now, it is not clear whether regimens specifically designed for older individuals (e.g. VABE, POCE, THP-CVP, CNOP, VMP, P-VEBEC, etc.) present any advantage over standard treatment with CHOP in terms of response and toxicity [8]. In the presence of cardiovascular disease, anthracycline-containing regimens should be avoided. Suggested regimens are then those without anthracyclines (e.g. CVP or COP) or those including the least cardiotoxic drug i.e. mitoxantrone.

The same intensive combination chemotherapy used for adults can probably be administered to patients between 60 to 70 years in the absence of organ function impairment [9]. For patients over 70 years of age, therapy should be started at the full dosage especially when, in case of neutropenic sepsis, G-CSF is available. Oral antibiotic prophylaxis may be a reasonable alternative. The tolerance of the first cycle of chemotherapy will then be a guide for the delivery of the rest of therapy.

## Ovarian carcinoma

A series of meta-analyses of randomised controlled trials raised the question of whether the multidrug combination was more effective than an optimal dose of the single agent carboplatin for women with advanced ovarian cancer. The final results indicate that there is no evidence that the combination cyclophosphamide, doxorubicin and cisplatin (CAP) are more effective than carboplatin [10]. CAP was instead shown to be more toxic. Carboplatin administered as a single agent is safe and it has been shown that elderly cancer patients will tolerate the same dose intensity as their younger counterparts [11]. Single agent carboplatin could then be considered as the standard treatment for those over 70 years of age. A high response rate has been show for paclitaxel given as a single agent with no apparent difference in the tolerance between old and young patients [12]. Since paclitaxel has an extensive non-renal clearance, it could be considered as a possible single-agent treatment in patients with impairment of renal function, that can develop increased carboplatin toxicity.

## Colorectal carcinoma

*Advanced disease*

Systemic chemotherapy with 5-FU or 5-FU plus leucovorin should not be denied to elderly patients because symptom palliation and an increase in survival can be achieved for those who respond. The addition of irinotecan may cause more diarrhoea and leucopenia then in younger patients [13]. The peculiar neurological toxicity of oxaliplatin added to 5-FU can be a problem for elderly patients.

Oral fluoropyrimidines such as capecitabine or uracil and ftorafur (UFT) could be used to increase compliance in fragile patients. This procedure should be carefully evaluated as the role of intrahepatic chemotherapy is still controversial and requires the placement of an intrahepatic catheter in patients with possible vascular problems. Even in the elderly, resection of selected liver metastases may result in a survival benefit.

*Adjuvant chemotherapy*

A significant advantage with 5-FU-based regimens has been demonstrated for stage C and to lesser extent for stage B2. In elderly patients treated with 5-FU a higher degree of mucositis, diarrhoea, bone marrow depression and cardiac toxicity can be expected. Treatment discontinuation has been shown to be higher after 70 years of age [14]. The weekly schedule of 5-FU and leucovorin administration, probably, can be better tolerated than the five daily administration once a month in elderly patients [15].

In patients with rectal carcinoma, preoperative or postoperative chemoradiation has become the standard, although older patients with rectal carcinoma appear to be at risk for higher bowel toxicity. The combined treatment should not be denied to non-fragile patients, while fragile patients should probably be treated with surgery and radiotherapy alone.

## Advanced bladder carcinoma

The standard chemotherapy for advanced bladder carcinoma, is methotrexate-vinblastine, doxorubicin and cisplatin (M-VAC). In elderly patients toxicity with this regimen has been found to be significant [16], although the response rate was superimposable to that obtained for younger patients. Less toxic regimens are required for older patients with bladder cancer. Gemcitabine which is relatively well tolerated in the elderly has recently been shown to have activity in this neoplasia and could therefore be considered as an alternative option, at least in fragile patients. Since the association of gemcitabine with cisplatin has been shown to produce similar response rates to those of M-VAC but with less toxicity, this combination could be used instead in older non-fragile patients [17].

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