



## INTERVIEW



**HANS WILDIERS**, Member of the European Medicines Agency's Geriatric Expert Group, discusses his interest in geriatric medicine and optimising treatments in older people with cancer

# Caring for older patients with cancer

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**Q: Could you tell our readers a bit about your background and how you became involved with medicines for older people?**

**A:** I am an internal medicine specialist by training, but already from the start of my career I had an interest in specialising in geriatric medicine. Unfortunately, there were no scientific research possibilities in the geriatric field at that time. While rotating on the oncology department, I also became increasingly interested in this rapidly evolving field and had a desire to improve the care for older patients with cancer where there was a high unmet need. I had the opportunity to undertake a PhD on tumour angiogenesis, which was very interesting, but my heart was more with the patients, so I was happy to pursue my clinical training in oncology and become a staff member at the department of general medical oncology at the University Hospitals Leuven in Belgium. I became involved in the breast cancer field and decided to focus my future research on breast cancer but also on the care for older persons with (breast) cancer. I realised that nearly half of the patients seen by the medical oncologist are "old". At that time, older patients were nearly never evaluated by geriatricians or geriatric nurses to investigate the presence of other healthcare problems besides the cancer. Together with Cindy Kenis, a nurse with the same interest, and with colleagues from the geriatrics department, we started large scientific projects to integrate geriatric assessment into the care of older persons with cancer.



We were able to publish a large amount of scientific publications on these studies, and we try to integrate these principles for all older persons with cancer. Besides that, I also initiated several clinical trials specifically for older persons with breast cancer.

Since 2018, I became president of the International Society of Geriatric Oncology (SIOG) whose mission is to bring the “geriatric/ holistic thinking” to all older patients with cancer and not just the few who come to a geriatric oncology consultation. One of SIOG’s major goals is that every oncologist should become a geriatric oncologist. They should be aware of the impact of comorbidities on cancer treatment and prognosis, how to perform a geriatric assessment and assess frailty, and how to optimise treatment for this fragile population. Overtreatment should be avoided, because older people derive less benefit from anticancer treatment in many situations compared with young cancer patients, and in some cases the harm of treatment is larger than the benefit. This needs to be balanced with undertreatment which can also be harmful. Sometimes adapted anticancer therapies can improve quantity and, more importantly, quality of life and this type of intervention should not be withheld from patients.

**Q: Can you tell us more about your role as a member of the European Medicines Agency’s Geriatric Expert Group (EMA GEG)?**

**A:** The EMA’s GEG consists of seven geriatricians and one non-geriatrician (me). The GEG’s goal is to ensure older patients are well represented in the drug approval process. Clinical study exclusion criteria often result in the fact that only the fitter, more healthy elderly patients qualify for drug trials. It is well known that during the registration process of new drugs there are few elderly subjects taking part in these studies which leads to a skewed and wrong vision on how these new drugs are tolerated and effective in the general, often non-fit older population. The EMA created the GEG to ensure these issues are recognised and to make sure that enough knowledge is available on new drugs for the non-fit population. Drug companies have the tendency to say their drugs are well tolerated in the elderly but, in most cases, they have not examined the drug effects in a frail population. The EMA has written several papers and a guideline for the industry on how they should report on their new drugs related to age. It is also recommended that some form of geriatric assessment is integrated in future registration clinical trials for the older subpopulation included in these studies. Unfortunately, these recommendations are not (yet) mandatory, and the pharma industry has few incentives to integrate them at present.

**Q: Drawing on your experience in geriatric oncology, what evolution or improvement in the design of drug development programmes have you seen with respect to this special population?**

**A:** In the past, there were often age cut-offs for clinical trials, so if you were 70 years or over, you were not allowed to participate. Fortunately, that attitude has strongly been discouraged and such cut-offs have been reduced, but, still, registration trials do not represent the frail population. There are several ways to deal with this in the future. One is to make the inclusion criteria of trials less strict because now you need to be built like an

Olympic athlete and your heart and kidneys need to be healthy. Also, significant comorbidities, which are often present in older persons, are an exclusion criterion for many clinical trials. Fortunately, there is a recent important publication from ASCO (the American Society of Clinical Oncology) proposing to make these inclusion and exclusion criteria for clinical trials more rational so that only those who are at high risk of an adverse outcome are excluded from participation. Secondly, the EMA or the US FDA can also require that safety studies in frail persons are performed after drug approval. The industry is quite resistant to perform such trials because it could generate negative publicity on the drug if severe side effects occur, sometimes but not always related to the new drug. The industry will rarely voluntarily perform such studies so we should develop procedures to make them happen.



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**Q: Would you like to see a geriatric regulation developed to encourage development of appropriate drugs [similar to the EU Paediatric Regulation which came into effect in 2007]?**

**A:** The goal of requesting more information on new drugs in frail people can be achieved by using a carrot or a stick. The stick could be that if a company doesn’t provide the post-approval evidence of the product’s effect in the geriatric population within three years after the initial approval, the registration will be withdrawn. The carrot strategy may work better, for instance, if a company delivers within three years the data from the geriatric population, an extension of the patent could be granted.

**Q: What would you advise the industry to be aware of when planning to file a marketing authorisation application for a product targeted at the older population?**

**A:** Companies should provide data on their new drugs for older persons and describe whether there is a different safety (and efficacy) profile in frail versus non-frail older people.

Secondly, for some scenarios, elderly-specific trials may be required, for example, if the standard of care in the young/ fit population is chemotherapy or surgery with significant side effects, you will never be able to recruit frail patients in a randomised study comparing standard therapy with a “lighter” therapy because physicians and patients will not accept the risk of being randomised in the control arm. Also, there may be



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settings where standard therapy is too harsh and aggressive (eg, allogeneic transplantation for leukaemia). A possible solution is to investigate two experimental arms that are expected to be tolerable by most frail patients.

Thirdly, observational studies and population registries can also teach us a lot on the effect of new therapies in the general/frail older population. Some caveats are present though. Observational studies on different treatment attitudes (eg, adjuvant chemotherapy in older women with breast cancer) within one country are often difficult to interpret. The group receiving adjuvant chemotherapy is certainly more fit than the group not receiving adjuvant chemotherapy, a phenomenon known as “selection bias”. Comparing these two groups could lead to the conclusion that chemotherapy survival is much better for the chemotherapy group, and that chemotherapy may even make older persons fitter, which is, of course, a wrong interpretation. But if you compare treatment patterns between different countries with different standards, more solid conclusions can sometimes be drawn. For example, there was a big difference in the use of adjuvant chemotherapy for older patients with breast cancer between the Netherlands and Belgium. In the Netherlands, where much less chemotherapy was given to old people with high risk tumours, the survival rate was lower than in Belgium, indicating undertreatment in the Netherlands. But on the other hand, for low risk tumours, more antihormonal therapy is given in Belgium, but does not impact survival. Antihormonal therapy can induce debilitating side effects, so overtreatment may have been present.

**Q: Do you think we need to develop a new way of categorising older people? For example, should it be based on the number of concomitant diseases and their severity rather than age?**

**A:** Yes, absolutely. Chronological age is a bad criterion to decide the therapy – biological age is a much better measure, reflecting the fitness of the person. How do we measure biological age? Geriatric assessment is considered the best way to measure this. It is a diagnostic process which considers multiple domains of health, including physical performance, cognitive wellbeing, depression, nutritional status, social status, evaluation of comorbidities and presence of geriatric syndromes (which are measured by a geriatric assessment).

What is the definition of frailty? The geriatricians tried to define this in the past. Despite the absence of global consensus on the exact definition and cut-off, there is consensus that frailty is a cumulative deficit disorder, where a higher and more severe deficit in the domains above indicates higher frailty level. The

extremes of fitness and frailty are very clear. A 75-year old who can run a marathon can generally tolerate standard therapy, while a wheelchair-bound severely demented 72-year old will not. However, most patients are more in the middle, with some deficits in some domains. Some older patients are fit and don't need a full geriatric assessment, which takes 30–40 minutes to evaluate. For this reason, European oncologists often use a short screening tool in all 70 years or older cancer patients where a treatment decision is needed.

The most popular screening tool is the G8 test, which consists of eight simple questions, which takes about two minutes to perform. About 30% of 70-plus patients with cancer have a good score on the G8, and don't require a full geriatric assessment since, in this case, it will rarely show severe other health problems. The other 70%, however, have a lower score, and geriatric assessment often shows underlying health problems in the domains mentioned before. Such a geriatric assessment is important for these patients; it demonstrates a high number of health problems which are, by the way, often not known by the treating oncologist. It also predicts tolerance of treatment and survival and has been demonstrated to influence oncological treatment decisions significantly.

It should be acknowledged that geriatric assessment is a process, not a single act. The detection of healthcare problems should also be assessed, and geriatric interventions should follow. For instance, if malnutrition is found, the cause should be sought, and a dietitian can often help to alleviate this problem. Oncologists are not specialised in these geriatric interventions, and therefore need collaboration with geriatricians, the general practitioner, dietitian, psychologist and other healthcare workers. These interventions will lead to better patient outcomes, since a holistic healthcare approach is key to successful outcomes, particularly in the elderly patient.

**Q: Regarding patient-centricity in special populations, could you foresee patient groups or professional organisations being involved in organising better care for older patients with cancer?**

**A:** The SIOG, founded in 2000, has been working intensively to foster the development of health professionals in the field of geriatric oncology for the optimisation of treatment of older adults with cancer. SIOG is a multidisciplinary team of oncology and geriatrics physicians, as well as allied health professionals and expert trainers with a unique collaborative approach to address the rising public health challenges related to ageing and cancer around the world. As of 2019, it has over 1,700 members in more than 80 countries. Patient advocates are active within SIOG. Najia Musolino is the current CEO and leads this organisation dynamically. SIOG recently provided an important publication on “Top priorities for the global advancement of cancer care in older adults”, under the guidance of Martine Extermann. This document has been submitted for publication, and addresses four priority domains: education, clinical practice, research, and collaborations/partnerships. It includes input not only from SIOG members, but also from extensive consultations with partners across the world. SIOG hopes that this document will offer guidance for international and national endeavours in providing adequate universal health coverage for older adults with cancer, a major and rapidly growing group in global epidemiology. ■