The “silver tsunami”, the clinical scenario with the increase of elderly cancer patients, is becoming, year after year, more and more concrete. Even more, it is shaping up to be a perfect storm in cancer treatment decisions. On the one hand, the escalation in the incidence of cancer diagnoses in elderly population setting leading to the raised incidence linked to the increase in life expectancy (indeed cancer is defined today as a chronic degenerative disease). On the other hand, a “conscious ignorance” in geriatric oncology. The “Achilles’ heel” of approach based on evidence-based medicine (EBM) is represented by the availability of this same evidence. Socket suggested the use of “the best external evidence” to guide clinical decisions. Unfortunately, elderly cancer patients are under-represented in clinical trials, especially the older (age range 75-84) and the oldest patients (>85). As undelighted by Cartabellotta, the absence of evidence can lead to decision-making paralysis because EBM does not require clinical decisions to be based on “best possible evidence”. This is probably the reason why a nihilistic approach classically winds among oncologists to treat elderly patients. Furthermore, to complicate this picture, the heterogeneity of this population is crucial, in fact it is simple either to find subjects very fit and subjects very frail enough not to be able to live independently. Obviously, these different scenarios play a decisive role in treatment results as efficacy and tolerance. All this overview helps us to understand why treating elderly cancer is still very tricky. We have demonstrated that there is a strong correlation between the comorbidities (reducing the functional organ reserve of the patient) and the possibility to have a beneficial effect by the oncological treatments bearing their toxicities. It is possible to deliver radiotherapy to a fit elderly patient safely and effectively for prostate cancer, for breast cancer, for NSCLC and in other types of tumours. Some other elderly patients can benefit from chemotherapy with oxaliplatin. It is not surprising that elderly gastrointestinal cancer patients tolerate a toxic chemotherapy regimen such as FOLFOX or XELOX.

As you can see, all evidence comes from retrospective or prospective studies, so it is extremely hard to apply it. The American Geriatrics Society recently encourages active recruitment of older adults, adds standard measures of function and/or frailty, and changes review criteria to ensure the health status of a study population mirrors typical clinical populations.

While we expect data from new RCTs, we have a great opportunity to modify the treatment cancer idea and therefore to personalize really the same treatment for each individual patient, trying to do “the right thing to the right person”.

The first step for this personalization process is obviously determining the biological age of the patient. Indeed, it is essential to treat patients according to their organ reserve. The patient should be treated in the best possible ways recalling the motto “primum non nocere”.

The second step is not to consider malignant tumour cell as the only focus for the treatment. Even today, the oncologists of different branches (chemotherapy, radiotherapy, and surgery) have a cancer centric view, so they use surgery, target therapy, chemotherapy and/or radiotherapy to kill tumour...
cells. It is demonstrable that in tumour mass the stromal cells represent the majority of cell types. A focus only on malignant tumour cells has been deemed inaccurate. It is necessary a global vision considering tumour mass with endothelial cells, fibroblasts, macrophages, neutrophils, dendritic cells, and cytotoxic T cells.

Since there is not a real EBM approach in geriatric oncology, this time can be the beginning of a cultural revolution that leads to review knowledge and thinking about cancer globally. Softly, this revolution is started introducing immune checkpoints inhibitors in clinical practice. Let’s begin, for example, with radiation oncology which is now losing the connotation of “tumour’ sniper” and gaining the role of modulatory tool that facilitates the recruitment and activation of the immune system to fight tumours.

The immune system of the elderly is different from that of a younger person. In the latter, it is more normal to find a hyperergic immune system differently than in the elderly. Therefore, it is reasonable to think that there are two macro-scenarios of tumour-host interaction: the first one is the most active immune system and the second one is the laziest immune system. Between the two extremes, there are obviously intermediate and remarkably heterogeneous situations. In our opinion, only by understanding which interaction takes place in the subject, one can optimize the therapeutic approach and reach to a real customization of the treatment.

A person with a lazy immune system must be stimulated to induce an immune cell mediated response. Normally the elder has a lazy immune system to arouse.

A recent study analysing 24 eligible randomised trials (including a total of 8157 younger and 6104 older cancer patients) highlighted that the survival benefit conferred by ICI was not age-dependent. In this context, it is necessary to make the most of the interactions of ICI with another oncological arm, for example with radiation therapy, which can act on several levels of this interaction. In our recent study, analysing the effect of the association of immune check point inhibitors and radiotherapy in non-small cell lung cancer, we concluded that combination increase the overall survival. If we analysed these data combining the effect for patients with age < or ≥ 65 years, there is no difference in OS between these two groups: 54.3% of 368 included patients with age ≥ 65 years and 50% of 464 with age < 65 years live at 1 year with a RR 1 (95% CI 0.76-1.33; \( p = 0.99 \)) (Figure 1). It is really a great opportunity to use all pragmatic evidence to increase the efficacy and effectiveness of immunological arms and to adjust the host microenvironment, where tumour growths, towards an anti-neoplastic response.

Age does not usually restrict the active treatment of cancer, but the patient’s other diseases and poor general condition do. Geriatric and psychosocial assessment of the patient’s situation help in making the treatment decisions. Close collaboration with other health professionals will be a tool providing adequate therapy to elderly patients with cancer in order to increase treatments’ effectiveness and to decrease cost. There are promising achievements in each of the requirements listed, but a huge, holistic effort has still to be made.

**Conflict of Interest**
The Authors declare that they have no conflict of interests.
References


