

Cancer immunotherapy: think of the elderly

Press release of the French National Academy of Medicine *

September 16, 2021

Immunotherapies, known as "checkpoint" inhibitors, have revolutionized cancerology. Currently, about twenty different cancers are likely to respond to this type of therapy. The specificity of immunotherapy is that it can induce long-lasting responses, or even complete remissions over several years after stopping immunotherapy, leading to reclassifying certain cancers as "chronic disease", which gives hope for a paradigm shift in cancerology.

In this context, it seems essential to be able to shed an objective light on their effectiveness and toxicity in elderly patients. Indeed, anti-cancer treatments are prescribed to them with a lot of reservations, even though more than 50% of oncology patients are aged 75 and over. This caution is based both on the a priori assumption of a poorer tolerance and a lower efficacy. However, these two factors remain to be studied according to the type of cancer and, above all, the individual modalities of ageing, that are very variable.

Unfortunately, patients over 70 years old are under-represented in randomized studies, mainly due to strict inclusion criteria regarding co-morbidities and also to a sometimes excessive fear of investigators to include elderly people. As a result, efficacy and safety clinical study results are often too limited to be taken into account in this subgroup of patients.

Melanoma is one of the first tumors for which immunotherapy was used. It therefore represents a good model with a history of use of more than 10 years.

The first clinical trials (ref 1,2) evaluating the efficacy and safety of immunotherapy in metastatic melanoma and other solid tumors in the elderly were published between 2016 and 2020, and included in a meta-analysis. Two large studies, involving 5265 and 10,669 patients respectively, show that patients over 65 of age respond as well to immunotherapy as younger patients with an identical relapse-free survival and overall survival, whatever the immunotherapy prescribed (ipilimumab, anti-PID-1, or even anti-PDL-1) without more side effects. A recent study from 2021 (ref 3) has the originality of including for the first time four cohorts of "real life data". It thus provides important new information for the day-to-day management of elderly patients with an indication for cancer immunotherapy. Indeed, there are no longer any exclusion criteria

related to comorbidity factors. It confirms that the efficacy of immunotherapy is similar to the rest of the treated population and, above all, that there are no more severe or different side effects.

Thus, the response to immunotherapy does not appear to be influenced by immunosenescence and the incidence of autoimmune diseases induced by this treatment is not higher in this population. This new information is particularly important as immunotherapy is now targeting tumors, such as advanced cutaneous squamous cell carcinoma and Merkel's tumor, which are skin tumors in people over 70 years old.

These results also raise the question of prescribing immunotherapy as an adjuvant in the elderly. For example, in melanoma, adjuvant treatment with anti-PD-1 has been shown to reduce the risk of relapse after lymph node dissection.

In this context, geriatric assessment takes on a very special role to ensure that there is no interference with some comorbidities, mental, emotional or nutritional conditions. The assessment of these multidimensional elements can indeed help the oncologist to even better define the benefit/risk ratio.

The National Academy of Medicine underlines the importance of:

1. treating patients over 70 years of age with cancer whenever there is a potential benefit for them;
2. collaborating closely with onco-geriatricians in the therapeutic decision and follow-up, taking into account all aspects of the elderly person;
3. continuing and increasing clinical and translational research on cancer immunotherapy in the elderly, with a view of enabling them to benefit from modern treatments that are the least toxic possible, without impairing their quality of life.

References:

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- 2- Samani A & al. Impact of age on the toxicity of immune checkpoint inhibition. *Immunother. Cancer* 2020;8: e000871. doi:10.1136
- 3- Iacono D & al. Immunotherapy for older patients with melanoma: from darkness to light? *Pigment Cell Melanoma Res.* 2021; 34:550-563

* Communiqué from the Academy's Rapid Communication Platform validated by the members of the Board of Directors on 15 September 2021.