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Hurrying up but not rushing, acting and not reacting, good sense and not common sense: open thoughts and reasonable doubts on COVID-19 vaccination strategies in cancer patients

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At the time of writing this editorial, it is almost one year since we entered the pandemic nightmare¹. “*At the time of writing*”. These five words have been a common cautionary warning in fields facing sudden changes, like financial journalism when dealing with news from stock exchanges. We, as clinical oncologists, use them for very special occasions such as “late-breaking abstracts” or rare scientific papers dealing with cutting edge science and breakthrough innovations. Nothing to do with the strength and robustness, balance and evidence that we have been taught to adopt when dealing with recommendations, guidelines and clinical decision making².

Now we're not only getting used to the “*at the time of writing*” expression, but we feel compelled to use it. When we had our first (virtual, obviously) meeting as authors of the present editorial our first concern was: is our view going to be up-to-date when available to readers?

That's how we are living the present constant state of emergency. What has this to do with science and data? We are constantly asked to give advices, make choices, recommendations and prescriptions. We are asked to be men and women of science. Doctors. We've been trying to do this since the end of February 2020, in a balance of pros and cons, with the same feeling of Philippe Petit while walking on a wire suspended between the tops of the Twin Towers. With the only difference that the life at stake was not *-only-* ours. At the time of the initial COVID-19 outbreak, clinical oncologists were asked for facing the issue on how to organize cancer care while dealing with the restrictions imposed by the first lockdown measures^{3, 4}. Many scientific societies have proposed critical recommendations^{5,6,7} for patients receiving active treatments, those in follow-up (out of active treatment), as well as for the admission of patients and their caregivers.

¹ Spiteri G, Fielding J, Diercke M, et al. First cases of coronavirus disease 2019 (COVID-19) in the WHO European Region, 24 January to 21 February 2020. Euro Surveill. 2020 Mar;25(9):2000178..

² Reames BN, Krell RW, Ponto SN, Wong SL. Critical evaluation of oncology clinical practice guidelines. J Clin Oncol. 2013 Jul 10;31(20):2563-8.

³ Lambertini M, Toss A, Passaro A, et al. Cancer care during the spread of coronavirus disease 2019 (COVID-19) in Italy: young oncologists' perspective. ESMO Open. 2020 Mar;5(2):e000759

⁴ Pietrantonio F, Garassino MC. Caring for Patients With Cancer During the COVID-19 Outbreak in Italy. JAMA Oncol. 2020 Jun 1;6(6):821-822.

⁵ ESMO STATEMENTS FOR VACCINATION AGAINST COVID-19 IN PATIENTS WITH CANCER <https://www.esmo.org/covid-19-and-cancer/covid-19-vaccination>

⁶ Position Paper on COVID-19 vaccinations in cancer patients from the Italian Associations AIOM, CIPOMO and COMU https://www.aiom.it/wp-content/uploads/2020/12/20201231_Vaccino_COVID_19_AIOM_CIPOMO_COMU_1.0.pdf

⁷ COVID-19 Vaccine & Patients with Cancer <https://www.asco.org/asco-coronavirus-resources/covid-19-patient-care-information/covid-19-vaccine-patients-cancer>

Everything was rather fast, and being citizens of the first affected Western country, we as Italians lived both the urgency and the responsibility of reacting promptly, conscious of moving our steps in an uncharted territory, but bringing the flashlight to enlighten the road for the others behind us.

Now the time has come for implementing vaccination strategies and therefore to tackle all the cancer-related questions. No data? No worries! Again: react, do it fast, use common-sense. But now there is one big difference: shortage. Shortage as a wide concept to be intended in different ways, from the simple lack of the products to the logistical difficulties in administering as many shots as possible in a restricted time frame.

In a few words, would you clinical oncologists recommend the COVID-19 vaccine to your patients? Yes, we would. Of course, we would. The problem is: who goes first? Which should be the main drivers of our choice? How to integrate those drivers in the risk categories already established and defined for the whole population by governments and authorities at National and regional levels? Since the very beginning of our discussion, we did have clearly in mind a specific subgroup of patients that may deserve our immediate attention and be given “top priority”. This may sound in contrast with the inspiring principle of “no one left behind” that guided the medical community over last months, but it is exactly what guided our discussion here in a strategy of optimizing the way for ultimately taking care of everyone. Before COVID-19 other disruptive innovations revolutionized oncology during last years⁸. Thanks to new therapeutic options we do have more and more patients alive, in a smooth transition from *long-lasting palliative* to *curative chronic* treatments. Many of these patients required huge efforts in terms of both medical (including human) and economic investments for achieving those results, and this hard-to-define pool of patients constitute a kind of precious reserve of inestimable value for the oncologic community and society as a whole. These patients and their lives are somehow priceless. And we need to make any possible effort to protect them. Careful here, it is not a different weight of one life compared to another, is only priority to vaccine access in a state of emergency with supply shortage. Is it easy to distinguish those patients? Not at all. We may use some examples and try to picture a blurred frame in shades of grey. What about a young woman that just started a neoadjuvant treatment for a locally advanced breast cancer? A mismatch repair deficient metastatic endometrial cancer in radiologic complete response after 3 months of treatment? A potentially resectable 65 years old man diagnosed with liver only metastatic colorectal cancer. How can any guideline or any specific recommendation encompass all the spectrum of the possible scenarios? Those scenarios where only the experience, the calm, clinical judgment can tell: we can't risk a diagnosis of COVID-19 in this patient. Is that for a specific clinical reason? For the real practical medical consequences? No, it is not. It's true that a higher risk of complications or death has been recorded in specific oncologic diseases, but the real consequences we should be afraid of are interruptions or delays and all the possible ethical and psychological implications for the patients and their families.

Vaccines are conceived to protect individuals and the community⁹. Keeping this in mind, as well as their fundamental role as soldiers at the front, most of the countries started the vaccination plan from physicians and healthcare workers. That's why all the three authors of these lines already got their shots. This point brings to the discussion table an additional piece for consideration: all patients that are going to be admitted as in-patients should be considered for the vaccination with

⁸ Markham MJ, Wachter K., Agarwal N, et al. Clinical Cancer Advances 2020: Annual Report on Progress Against Cancer From the American Society of Clinical Oncology. J Clin Oncol 2020 38:10, 1081

⁹ Frederiksen LSF, Zhang Y, Foged C, Thakur A. The Long Road Toward COVID-19 Herd Immunity: Vaccine Platform Technologies and Mass Immunization Strategies. Front Immunol. 2020 Jul 21;11:1817.

some degree of priority. This is in line with a second level of protection, that looks more at containing possible spreads in centers for cancer care.

As third point we may try to define an additional large group of patients as a-not-to-prioritize category. Those out of active treatments, no evidence of disease and with low risk of relapse. Additional levels of complexity for further refinement and depending on the degree of shortage suffered by a single reality may consider at lower risk patients with no evidence of disease, but on active treatments with no immunosuppressive effect and low risk of relapse (i.e. adjuvant hormonal therapies).

What about the most difficult scenario? As oncologists we know that even for enrolling patients in clinical trials we have to make one the most difficult evaluations: life-expectancy¹⁰. We always struggle with that concept. It is such an ethical, human and clinical challenge that most of us are exhausted by. It goes far beyond the COVID-19 emergency. It is a question coming in different nuances from patients, relatives, colleagues, authorities, and many others. How and how much should the concept of life-expectancy be taken into consideration when balancing pros and cons of recommending the vaccine? To an advanced cancer patient. In the middle of a pandemic. In a moment of supply shortage.

From a more general perspective, further considerations may include the evaluation of the level of virus circulation and transmission within a specific area/community and may even go to additional levels of complexity including type of vaccine available and the prevalence of specific variants.

In the last weeks we witnessed an understandable pressure for prioritizing access to vaccine for anyone who have ever had a cancer diagnosis. That goes with obvious social and political implications.

The Italian philosopher Antonio Gramsci introduced the distinction between common sense and good sense¹¹. The first comprised the diffuse, uncoordinated features of a general form of thought common to a particular period and a particular environment. It contains what Gramsci named a "*healthy nucleus of good sense*" which, according to his thought, deserves to be made more unitary and coherent.

Keeping in mind that concept we believe that a rushed reaction moved by common sense like "every cancer patient should be vaccinated with top priority" should rather be a fast action moved by good-sense. We are hereby sharing our thoughts and doubts hoping that may help readers, colleagues, policy makers in their forthcoming difficult decisions.

¹⁰ Verduzco-Aguirre HC, Gomez-Moreno C, Chavarri-Guerra Y, Soto-Perez-de-Celis E. Predicting Life Expectancy for Older Adults with Cancer in Clinical Practice: Implications for Shared Decision-making. *Curr Oncol Rep.* 2019 Jun 25;21(8):68.

¹¹ Coben D. Common Sense or Good Sense? Ethnomathematics and the Prospects for a Gramscian Politics of Adults' Mathematics Education. <https://www.nottingham.ac.uk/csme/meas/papers/coben.html>