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VACCINATION CAMPAIGN ANTI COVID-19: TOWARDS RECOVERY

MEETING WITH FRANCO LOCATELLI, PRESIDENT
OF THE ITALIAN NATIONAL HEALTH COUNCIL AND
COORDINATOR OF THE SCIENTIFIC TECHNICAL
COMMITTEE

INFN promoted and organized last 22th March the webinar “Vaccination campaign anti CoViD-19: towards recovery”. Introduced by INFN president Antonio Zoccoli, the seminar has been held by Franco Locatelli, president of the Italian National Health Council and recently appointed as coordinator of the Scientific Technical Committee which supports the Italian Government in the management of CoViD-19 sanitary emergency. The meeting, dedicated to INFN community, has been organized to take the stock of the situation on contagion diffusion and on the evolution of the pandemic, in particular in our country. It was a moment of information and discussion on the vaccination plan. Here is proposed a summary of the main topics of the seminar. The full recording of the seminar [in Italian] can be found on the web page “Emergenza CoViD-19”, on the Institute website, dedicated to INFN community. [Here is the direct link](#)

The current scenario from an epidemiological point of view

I will start by presenting some data. To give you an idea of the global numbers, yesterday [21th March, ed] on the website of the John Hopkins Coronavirus Resource Center there were 123,308,000 cases of people infected by SarsCov-2, the whole globe was substantially affected by this pandemic. The other very sad fact is that unfortunately there are already more than 2,716,000 people in the world who have lost their lives, with extraordinarily high numbers in the United States, in Brazil or Mexico. However, as you well know, about 105,000 people have lost their lives by now even in Italy. If you will allow me a personal observation, I am from Bergamo, and this number is exactly equivalent to the population living in the city where I was born. Looking at the ECDC (European Centre for Disease Prevention and Control) data, more or less the whole of Europe is still affected by the circulation of the new Coronavirus, with some areas, such as Central Europe, particularly affected by the epidemic spread.

We have proof of how Italy is hit by what can be defined as a third wave: in terms of new infections, there is nevertheless a deceleration of the curve and perhaps even a reduction; this week we had 2,600 fewer

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cases compared to those observed the week before. But the burden on intensive care units (ICU) is extremely high: the occupation of beds in intensive care units, now at 36%, has a 30% critical threshold, above which a whole series of other activities requiring the support of ICU beds are interrupted, or have a significant slowdown.

I can give you two more pieces of information: the average age of people affected by COVID-19 is 47 - whilst the median age of people who lose their lives is just over 80 - and there have been around 127,000 health workers affected.

Most common indicators of the infection's trend

On the matter of indicators, I would just like to comment on the 7-day cumulative incidence function, which has recently been added as an indicator for determining risk class assignment. Overall, the country had a cumulative incidence of exactly 250 cases in the week from March 8 to 14, which is the threshold that had been set to determine the automatic move into the red zone. Basically, there is a very large number of regions that have numbers well above this threshold. Another way of presenting the epidemic situation in the country is to look at the municipalities that have not been affected by a single case in the last 14 days, from March 1 to 14, which are very few and almost all located in Sardinia, and this explains why Sardinia was assigned the so-called white zone.

As a matter of fact, the increase in cases in the so-called third wave has affected all age groups. What has been observed, unlike in the past, is also an increase in the population aged between 0 and 18. From a purely biological point of view, this is due to the fact that the so-called UK variant is more contagious in the paediatric population, but I would like to make it quite clear that this does not translate into a greater severity of cases in those aged 18 or younger.

We previously spoke of deaths, sadly, but before getting on to the vaccines let me walk you through what the increase in mortality compared to the previous five years has been. Looking at the data from ISTAT you can clearly see that in northern Italy, especially in Val d'Aosta, Piedmont, Lombardy and the autonomous provinces of Trento and Bolzano, there has been the greatest increase in deaths compared to the previous five years.

COVID-19 represents the fourth most frequent cause of death in the country and, I believe, this gives a good idea of how dramatic the impact of the SarsCoV-2 pandemic has been worldwide. Obviously, Italy is no exception.

Assessment of the impact of the pandemic

In order to properly estimate the impact of the Covid-19 pandemic, it is perhaps worth talking about what

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the indirect impact is, and I do so by using two diseases in particular as examples: cardiovascular diseases and blood cancer diseases. Regarding cardiovascular disease, SarsCov-2 can cause direct and indirect damage to the body. However, there are also indirect effects pertaining to a reduction in hospitalisations for cardiovascular diseases, which in turn results in an increase in so-called indirect mortality, also in connection with a reduction in non-urgent medical procedures and cardiovascular prevention strategies. Compared to the previous year, the Federation of Italian Cardiologists (IFC) has documented, for example, almost a fourfold increase in the case fatality rate for acute myocardial infarction and this shows how the pandemic has also substantially caused a series of indirect deaths linked to pathologies for which all systems of timely diagnosis and equally rapid treatment have, in some way, been lacking. If we refer to the number of out-of-hospital cardiac arrests observed last spring, there is a clear increase in 2020 compared to what was observed in the previous year, in a clear correlation with the number of cases of COVID-19. Speaking of cancer, unfortunately, it must be acknowledged that both surgical and chemotherapy or radiation treatments have been cut back, and even cancelled, in order to reallocate staff to treating COVID-19 patients. Above all, we must be aware that for some cancers - bladder, breast, colon or head and neck - delaying treatment increases the risk of a poor outcome.

Then there is the big issue of screening. The National Cancer Institute (NCI) in the United States, for example, predicts that over the next 10 years there will be 10,000 more deaths from breast cancer or from colorectal cancer, and in the United Kingdom mortality is expected to rise by almost 17% for colorectal cancer and 10% for breast cancer. It is therefore clear that we need to get out of this critical situation as soon as possible in order to re-establish a whole series of activities that will also cancel out this effect on mortality, indirectly caused by the pandemic. The only way to do so is to have vaccines and, most of all, to vaccinate as many people as possible. On top of the the non-pharmacological containment and mitigation measures that we have extensively learned in recent months, from interpersonal distancing to the use of personal protective equipment, rather than frequent hand washing and the avoidance of gatherings, the only way to eradicate or at least contain an infectious disease, making it endemic, with a low mortality impact, is to adopt broad vaccination strategies, mass vaccination campaigns. Let me remind you that it is precisely thanks to the use of vaccines that we have been able to eradicate smallpox worldwide, just as there are no longer any cases of polio in Europe.

Vaccines currently in use around the world and how they work

There are four vaccine platforms that have been developed. There are vaccines based on dead or attenuated viruses: the model, as an example, is polio, and one of these vaccines is the so-called Sinovac vaccine developed in China. Then there are vaccines based on the spike protein combined with

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an adjuvant to increase its immune response power. Finally, there are two definitely innovative platforms. The first is based on the use of a viral vector, for which a harmless non-replicating virus (essentially an adenovirus). Before the COVID-19 pandemic, this type of vaccine platform had only been developed for the Ebola virus, whereas vaccines based on nucleic acids, particularly RNA, are completely new. The two examples of vaccines that have already become available in our country are the RNA vaccines developed by Moderna and Pfizer Biontech.

I think it may also be useful to look at what has been the investment of various countries in the development of candidate vaccines. Twenty-seven vaccine candidates have been developed in the United States, sixteen in China, and then down to single-digit numbers for all the other countries. Italy currently has two candidate vaccines in various stages of development. The development phases basically first refer to the design of the vaccine according to one of the four vaccine platforms I mentioned earlier, then to the execution of studies on animals and then to the execution of studies according to what are called boot clinical practices in different phases: phase one, phase two and phase three, before arriving at its market launch and use in large numbers, once a vaccine has been approved.

What is essentially common to all vaccines? The fact that they trigger an immune response of what we can define as the adaptive immune system, represented by B-lymphocytes, which produce antibodies as they mature into plasma cells, and by T-lymphocytes, which play a facilitating role in the development of the immune response, as well as generating cytotoxic populations in the cells that become infected by a given viral pathogen, in our case SarsCov-2. For example, in RNA vaccines, once injected, the cells are penetrated by this RNA with the subsequent production of proteins that are picked up, digested by the antigen-presenting cells, which are physiologically responsible for triggering both an humoral or cellular immune response.

Differences between different vaccines in terms of storage, numbers and intervals of doses to be administered

I would like to try to share with you some further thoughts on the vaccines and to do so we should start with an observation. Thirteen vaccines have been approved in various parts of the world and four are currently approved in Italy and EU: they are the Pfizer-BionTech RNA vaccine, the Moderna RNA vaccine, and the two vaccines I referred to earlier, which use an adenoviral vector to carry the genetic information inside the cells. The latter are the AstraZeneca's vaccine, which is based on a chimpanzee adenovirus, and the Johnson & Johnson's vaccine, which is based on a human adenovirus. The so-called Sputnik vaccine is also a vaccine based on the use of adenoviral vectors, with the peculiarity - all these four vaccines require two administrations to generate a complete immune response - that in the Sputnik

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vaccine the adenovirus used for the first administration, which we could almost define as priming, differs from the second, which is instead defined as a vaccine boost.

Both the approved Pfizer BioNTech and Moderna vaccines require two doses: Pfizer BioNTech at 21-day intervals, Moderna at 28-day intervals. The maintenance, or storage, conditions differ. Those of Pfizer BioNTech's vaccine are more challenging, because it must be kept between -60°C and -80°C , it can withstand five days at a temperature between 2°C and 8°C and it should not be kept at room temperature for more than two hours. The storage conditions for Moderna are more favourable: it must be kept between -15°C and -25°C , it has a stability of one month between 2°C and 8°C and it substantially resists without alteration for 12 hours at room temperature. What is the efficacy of these vaccines? It is resoundingly high: 100% for both after the second dose.

Here is some information on the other two approved vaccines. The Johnson & Johnson vaccine was approved on March 11 by the European Medicines Agency (EMA) and a couple of days later by the Italian Medicines Agency (AIFA), but the first doses will arrive in the country in April. It requires only one dose, which makes it unquestionably attractive precisely because it results in immunisation with only one dose. In the case of AstraZeneca, the best immunisation results were observed when the two doses were 12 weeks apart. This can be explained by an immunological observation, because a too close administration risks generating an immune response against the adenoviral vector, which somewhat reduces the vaccine's immunising capacity. Once again, with respect to the severe forms of the disease, the protection is extraordinarily high. As far as AstraZeneca is concerned, you will certainly have noticed that it has not yet been approved by the US Food and Drug Administration.

Then there are vaccines based on the use of the spike protein with a neo-adjuvant. Novavax will in fact be submitted for evaluation by the EMA very soon and, here too, the vaccine involves two doses, ease of storage between 2°C and 8°C up to six months. Preliminary data that have been shared show significant efficacy for the Novavax vaccine as well. The one based on an inactivated virus is for example the CoronaVac vaccine, again with two doses two weeks apart. If we look at the list of countries where there has been approval for emergency use, we see that parts of the globe, especially in South America and in China, have had a widespread use of this vaccine platform.

The vaccination plan

This is what I think is a crucial point, namely the priorities regarding who to vaccinate. As you know, in our Country the choice was made to initially give priority to health workers and then to people living in Nursing Homes, before those who work there, and then to the over 80s. Regarding health workers, it is my personal opinion that getting vaccinated is an essential prerequisite for exercising the profession, because those who go to hospitals or Emergency departments must have the assurance that everything

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reasonably possible has been put in place to avoid the risk of infection. On the question of why we should vaccinate patients over 80, the observation I made earlier suffices: the median age of people who have died is just over 81, so immunising them obviously means saving the loss of many lives. It is clear that the aim is precisely to reduce mortality, because what we know for sure is that the available vaccines confer protection against the disease, while it is still a matter of some debate as to whether they offer complete protection in terms of preventing contagion. The vaccines we have provide immunity from disease, but we do not fully know whether they provide a sterilising immunity; it is possible that some vaccinated subjects may potentially become infected, but they will certainly no longer develop the more dangerous forms of COVID-19, specifically because of the data on efficacy with respect to serious forms of the disease. Moreover, this uncertainty about sterilising immunity justifies the reason why the use of personal protective equipment is also recommended for vaccinated subjects. I mentioned earlier some data showing the effectiveness of the vaccination campaign in the Country: since the start of vaccinations, the outcome, in terms of growth in the number of cases, differs dramatically between healthcare workers and the normal population, because we now see very few cases amongst healthcare workers. Therefore, the 126,000 cases I mentioned earlier, practically all, belong to the period before the vaccine campaign. Even the data on protection for residents in assisted living facilities, if you look at the percentage of outbreaks out of the total reported in the Nursing Homes after the start of the second vaccinations, once again, the number of cases drops dramatically. All of which obviously provides further confirmation of the effectiveness and appropriateness of the vaccines.

Current evidences of the efficacy of vaccines globally

Yesterday [21th March, ed] in the United Kingdom where, there have been lockdown measures, but above all there has been an extraordinarily high number of vaccinated people, the number of people who lost their lives was 17. On 26 January, so basically less than two months ago, we were exactly two logarithms above that because we were at 1600 deaths recorded in the UK.

An article published on Cell, no more than five days ago, summarises the cumulative incidences of SarsCov-2 infection in subjects vaccinated with either Pfizer's vaccine or Moderna's vaccine, compared to the control group that received a placebo in the phase three study. By observing the data, you can see that already at 10-12 days after the administration of the first dose, the curves open up markedly like scissors, thus determining a clear demonstration of the efficacy of the vaccines. Curves of this type are very rarely observed and can rightly be described as a demonstration of the extraordinary effectiveness that biology and medicine have had in developing vaccines in less than a year to begin the vaccination journey.

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Variants of the virus and the persistence of vaccine protection

The so-called UK variant is known for its greater rate of contagion, but the data on the possible lethality have yet to be consolidated. You may also have heard of the Brazilian and South African variants: it is a sort of physiological phenomenon, that some strains emerge with nucleotide mutations and consequently amino acid mutations of the spike protein, particularly the part that binds to the receptor. I am not one of those who think that these variants can really determine resistance to vaccines; there is research that does not confirm this hypothesis at all, even documenting results in the opposing direction.

On the other hand, what do we not yet know in full? We do not know how long the protection will last; therefore, we do not know whether we will need booster vaccinations and how often.

Just this morning [21th March, ed] I saw a scientific study documenting that while in the healthy population there is already a resoundingly high level of protection after the first dose, in cancer and blood cancer patients protection of over 85-90% is only obtained after the administration of the second dose: after the first dose these subjects have a level of protection in terms of antibody response that is no more than 20%.

Lastly, the other point refers to the ability of vaccines to induce a sterilising immunity. The data on the sterilising capacity still need to be assessed, analysed, and consolidated in order to draw definitive conclusions. But we certainly know that they give a formidable protection against disease. ■