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COVID-19 Vaccination for Cancer Patients, What Oncologists and Cancer Patients Need to Know?

Humaid O. Al-Shamsi[1-4]*, Mona Abdullah Alfares[5] and Sadir Alrawi[1]

[1]Department of Medical Oncology – Burjeel Cancer Institute – Burjeel Medical City, Abu Dhabi, United Arab Emirates

[2]Innovation and Research Center – Burjeel Cancer Institute – Burjeel Medical City, Abu Dhabi, United Arab Emirates

[3]College of Medicine, University of Sharjah, Sharjah, United Arab Emirates

[4]Emirates Oncology Society, Dubai, United Arab Emirates

[5]Department of Infectious disease, King Abdulaziz University Hospital, Jeddah, Saudi Arabia

SUMMARY

As the current evidence is accumulating in support of multiple COVID-19 Vaccine in general population and the final regulators approvals are still pending, Multiple vaccine candidates have already received temporary authorization for emergency use. The mRNA vaccines are new to the clinical practice and global regulators have to balance the lack of medium to longer-term data on these novel mRNA COVID-19 vaccines. The inactivated vaccines have been used in cancer patients in the past with excellent safety profile and they may be theoretically the safeties vaccine for cancer patients. Currently there are no formal COVID-19 vaccine trial designed specifically for cancer patients. Some of the current major trials excluded cancer patients while others did not explicitly excluded malignancies. Early reports indicates that some cancer patients were able to enroll in some of the vaccine trials, yet no clear information if these patients were on active systemic therapies or surveillance. There is a need for a dedicated COVID-19 vaccine trials for cancer patients. The UK Independent report by the " Joint Committee on Vaccination and Immunisation for the Priority groups for coronavirus (COVID-19) vaccination"; Recommended "bone marrow and stem cell transplant recipients and people with specific cancers" to receive priority vaccination, without further clarification which "specific cancers" were referred to. Until further data are available, recommendations for vaccination for SARS-CoV-2 for cancer patients can not be routinely recommended. At the current time evaluation of cancer patients who wish to consider COVID-19 vaccination should be done in the context of clinical trials, if there is no access to clinical trials; This should be addressed "case by cases" basis with clear discussion about potential benefits, risks and uncertainties surrounding COVID-19 vaccination for cancer patients at the current time.

***Corresponding author**

Humaid O. Al-Shamsi, MD, MRCP (UK), FRCP(C), FACP, Burjeel Cancer Institute – Burjeel Medical City P.O. Box: 9054, 28th Street Mohammad Bin Zayed City, AbuDhabi, UAE, Tel Number: +97150-631-5388, E-mail: Humaid.Al-Shamsi@medportal.ca; alshamsi@burjeel.com

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Introduction

As the race for COVID-19 vaccination continues for the general population with more than 300 vaccine candidates in development, many in the final stages of clinical trials and some have already received temporary authorization for emergency use in some countries; as the vaccine's quality, safety, and performance data were acceptable, and that the benefits outweigh the foreseeable risks and uncertainties in the context of a public health emergency of international Concern [1-3]. The remaining question regarding COVID-19 vaccination for special population like immunocompromised cancer patients remains unanswered. In this review we will address the important aspects related to COVID-19 main vaccine candidates that are important for oncologists and cancer patients.

Current Main Vaccine Candidate's Mechanism of Action: Inactivated COVID-19 Vaccine Candidates

Conventional vaccines usually contain inactivated disease-causing organisms or proteins made by the antigens, which work by mimicking the infectious agent. The antigens stimulate the body's immune response, so it is primed to respond more rapidly and effectively if exposed to the infectious agent in the future and in this case the SARS CoV 2 virus [4]. Inactivated vaccines usually do not provide immunity (protection) that's as strong as live vaccines, so several doses over time (booster doses) are usually needed in order to get ongoing immunity against diseases. Inactivated vaccines are widely used to protect against: Hepatitis A, Seasonal influenzas, Polio and Rabies [5].

Sinopharm's vaccine candidate used the inactivated SARS-CoV-2 vaccine (Vero cell) with 2 doses schedule at day1 and a booster dose at day 21 [6]. The Oxford /AstraZeneca's (AZD1222) inactivated vaccine candidate, formerly known as ChAdOx1 nCoV-19, is made from a virus (ChAdOx1), which is a weakened version of a common cold virus (adenovirus) that causes infections in chimpanzees, that has been genetically changed so that it is impossible for it to grow in humans [7]. Genetic material has been added to the ChAdOx1 construct, which is used to make proteins from the SARS-CoV-2 coronavirus called Spike glycoprotein (S). This protein is usually found on the surface of SARS-CoV-2 and plays an essential role in the infection pathway of the SARS-CoV-2 virus [7]. The interim analysis of clinical trials of AZD1222 in the UK (COV002) and Brazil (COV003) showed the vaccine was highly effective in preventing COVID-19, the primary endpoint, and no hospitalisations or severe cases of the disease were reported in participants receiving the vaccine. There were a total of 131 COVID-19 cases in the interim analysis. One dosing regimen (n=2,741) showed vaccine efficacy of 90% when AZD1222 was given as a half dose, followed by a full dose at least one month apart, and another dosing regimen (n=8,895) showed 62% efficacy when given as two full doses at least one month apart. The combined analysis from both dosing regimens (n=11,636) resulted in an average efficacy of 70%. All results were statistically significant (p<=0.0001) [8].

The Sputnik V Russian vaccine which uses two different human adenoviral vectors. The second interim analysis of clinical trial published on November 24th 2020 data showed a 91.4% efficacy for the sputnik v vaccine on day 28 after the first dose; vaccine efficacy is over 95% 42 days after the first dose [9].

The new RNA SARS-CoV-2 Vaccine Candidates

The new RNA vaccines use a different approach that takes advantage of the process that cells use to make proteins: cells use DNA as the template to make messenger RNA (mRNA) molecules, which are then translated to build proteins [4]. An RNA vaccine consists of an mRNA strand that codes for a disease-specific antigen. Once the mRNA strand in the vaccine is inside the body's cells, the cells use the genetic information to produce the antigen. This antigen is then displayed on the cell surface, where it is recognised by the immune system [4].

Researchers have studied investigational mRNA-based therapeutic antibodies and therapeutic cancer vaccines in the past. A published phase 1 results from the first prophylactic mRNA vaccine clinical trial, for a candidate against rabies, was published less than 3 years ago [10,11]. Up until December 2, 2020, no mRNA vaccine, drug, or technology platform, had ever been approved for use in humans, and before 2020, mRNA was only considered a theoretical possibility for effective use in humans [12,13]. Also up until December 2, 2020, there were two novel mRNA vaccines awaiting emergency use authorization as potential COVID-19 vaccines, MRNA-1273 from Moderna, and (BNT162b2) from a BioNTech/Pfizer partnership [12]. Both have disclosed efficacy rates of more than 90%, higher than many had expected from vaccines developed so quickly. The vaccines' full safety data has not yet been published [5]. On December 2, 2020 the Medicines & Healthcare Products Regulatory Agency (MHRA) in the U.K. has granted a temporary authorization for emergency use for BioNTech/Pfizer's COVID-19 mRNA vaccine (BNT162b2), against COVID-19. This constitutes the first Emergency Use Authorization following a worldwide Phase 3 trial of a vaccine to help fight the pandemic [2].

Cancer Patient as Special Population

As the development of antibody responses following natural infection or vaccination is likely to be a key parameter in preventing and controlling COVID-19 pandemic, it is critical to understand these responses in vulnerable groups such as cancer patients [14].

In cancer patients, active immunization has been shown to confer protective immunity against several infections at similar rates to healthy individuals, which has translated into decreased duration and severity of infection and potentially improved morbidity and mortality [15]. In a meta analysis included 16 studies; patients with solid and hematological tumors were able to mount a serological response to inactivated influenza vaccine, meanwhile, influenza vaccine appears to be safe in these patients [16].

Another recent retrospective study evaluating if inactivated flu vaccine exacerbates immune events in patients treated with immune checkpoint inhibitors, it concluded that there was no increase in incidence or severity of immune-related adverse event was detected in patients on immune checkpoint inhibitors who received the inactivated influenza vaccine [17].

A recent study evaluating the SARS-CoV-2 antibody responses in patients infected with SARS-CoV-2 and with pre-existing aggressive haematological malignancies demonstrate that these patients can generate antibodies to SARS-CoV-2 antigens that are similar to those previously identified in COVID-19 patients without haematological malignancies [14]. The dynamics of antibody responses were broadly similar to that reported for the general population, except for a possible delay to seroconversion [14]. While these conversion rates are similar to those reported in patients without haematological malignancies the production of anti-N IgG in patients with hematological malignancies appears delayed; 50% seroconverted by day 28 compared to 90% of healthy individuals [14,18].

Cancer Patients in the Current Covid-19 Main Vaccine Trials

There are no confirmed information on how many people living with cancer, or with a history of cancer, have been involved in COVID-19 vaccine trials so far. But some cancer patients have been able to take part in these trials, although who can take part varies from trial to trial which we will try to address this by evaluating the major trials exclusion criteria [19]. Currently none of the main clinical trials that have been published included cancer patients including Oxford /AstraZeneca or Sinopharm candidates [20,21]. And both trials explicitly excludes anyone with a history of cancer [4,6]. Sinopharm inactivated vaccine trial, exclusion number 11 excluded malignant tumors [6]. The Oxford /AstraZeneca protocol exclusion number 7 [22].

History of primary malignancy except for

a. Malignancy with low potential risk for recurrence after curative treatment (for example, history of childhood leukaemia) or metastasis (for example, indolent prostate cancer) in the opinion of the site investigator.
b. Adequately treated non-melanoma skin cancer or lentigo maligna without evidence of disease
c. Adequately treated uterine cervical carcinoma in situ without evidence of disease
d. Localized prostate cancer

The Russian Sputnik V vaccine excluded the following as per the protocol [11]: Immunosuppressors therapy finished within

3 months before the enrollment. The Moderna candidate of the mRNA-1273 SARS-CoV-2 Vaccine in Adults Aged 18 Years and Older outlined the following exclusions criteria [23].

Immunosuppressive or immunodeficient state, asplenia, recurrent severe infections (HIV positive participants with CD4 count ≥350 cells/mm3 and an undetectable HIV viral load within the past year [low level variations from 50-500 viral copies which do not lead to changes in antiretroviral therapy [ART] are permitted]). Has received systemic immunosuppressants or immune-modifying drugs for >14 days in total within 6 months prior to Screening (for corticosteroids ≥ 20 mg/day of prednisone equivalent) [24]. The exclusion criteria has not explicitly excluded malignancies as other trials and preliminary unconfirmed initial information that the Moderna trial included 1500-2000 patients with cancer, the important question remains are these patients with active cancer on active treatment or cancer survivors on surveillance ? this remains to be answered. BioNTech/Pfizer involved healthy people aged 18 to 55 or 65 to 85. People with pre-existing conditions were able to take part as long as they did not require a significant change in therapy or hospitalisation for worsening disease in the 6 weeks prior to enrolment [1]. In later phases of the trial (phases 2 and 3) the lower age limit was reduced to 16 years old and individuals identified as being in a 'high-risk' group based on their use of public transport, being a frontline essential worker or other factors were included. Although people with cancer were not explicitly excluded from this list, those who are immunocompromised or receiving immunosuppressive therapy were not able to take part, and anyone taking part needed to have stable disease prior to enrolment [1]. The exclusions criteria as per the protocol [25].

Individuals who receive treatment with immunosuppressive therapy, including cytotoxic agents or systemic corticosteroids, eg, for cancer or an autoimmune disease, or planned receipt throughout the study. If systemic corticosteroids have been administered short term (<14 days) for treatment of an acute illness, participants should not be enrolled into the study until corticosteroid therapy has been discontinued for at least 28 days before study intervention administration. Inhaled/nebulized (except for participants in Phase 1 – see exclusion criterion 14), intra-articular, intrabursal, or topical (skin or eyes) corticosteroids are permitted.

Following the UK MHRA temporary authorization for emergency use for BioNTech/Pfizer's COVID-19 mRNA vaccine (BNT162b2) on December 2nd 2020, The Independent report by Joint Committee on Vaccination and Immunisation "the Priority groups for coronavirus (COVID-19) vaccination". The committee's advice is to offer vaccination to those aged 65 years and over followed by those in clinical risk groups aged 16 years and over. The risk groups identified by the committee included "bone marrow and stem cell transplant recipients and people with specific cancers", without further clarification which "specific cancers" [26].

Conclusion

As the current evidences are accumulating in support of multiple SARS-CoV-2 Vaccine in general population. While the final regulators approvals are still, multiple vaccine candidates have already received temporary authorization for emergency use. The mRNA vaccines are new to the clinical practice and global regulators have to balance the lack of medium to longer-term data on these novel mRNA COVID-19 vaccines. The inactivated vaccines have been used in cancer patients in the past with excellent safety profile and they may be theoretically the safeties vaccine for cancer patients. Currently there are no formal COVID-19 vaccine trial designed specifically for cancer patients. Some of the current major trials excluded cancer patients while others did not explicitly excluded malignancies. Early reports indicates that some cancer patients were able to enroll in some of the vaccine trials, yet no clear information if these patients were on active systemic therapies or surveillance. There is a need for a dedicated COVID-19 vaccine trials for cancer patients. The UK Independent report by the " Joint Committee on Vaccination and Immunisation for the Priority groups for coronavirus (COVID-19) vaccination"; Recommended "bone marrow and stem cell transplant recipients and people with specific cancers" to receive priority vaccination, without further clarification which "specific cancers" were referred to. Until further data are available, recommendations for vaccination for SARS-CoV-2 for cancer patients can not be routinely recommended. At the current time evaluation of cancer patients who wish to consider COVID-19 vaccination should be done in the context of clinical trials, if there is no access to clinical trials; This should be addressed "case by cases" basis with clear discussion about potential benefits, risks and uncertainties surrounding COVID-19 vaccination for cancer patients at the current time.

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