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Title: **Systematic Review of the SARS-CoV-2 Viral Vector Vaccine AstraZeneca (Azd1222)**

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Systematic Review of the SARS-CoV-2 Viral Vector Vaccine AstraZeneca (Azd1222)

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Abstract

It has been more than two years since the spread of the COVID-19 pandemic all over the world. Scientists still are in search of a permanent treatment and cure of this infectious disease. In this regard, on 20th April, 2020, AstraZeneca in collaboration with the Oxford University came up with a recombinant adenovirus-based vaccine labeled as "ChAdOx1 nCoV-19" or "AZD1222". Approximately, 22 viral vector-based vaccines are in the trial stage and ChAdOx1 nCoV-19 falls under the category of non-replicating viral vector-based vaccines. During vaccine development, ChAdOx-1 vector was specifically designed by red lambda recombination of Y25 serotype (chimpanzee) with HAdV-C5 serotype (human). In July 2020, clinical trials were initiated but due to some controversial side effects, these trials were halted for a while and resumed later on. AstraZeneca has been reported to generate both humoral and cell mediated immune responses. This vaccine exhibited 63% efficacy with few side effects. It also exhibited dwindling efficacy against the emerging variants of COVID-19. Since then, heterologous prime boost vaccination has been initiated, exhibiting elevated efficacy. Until now, 42.6% population of the world has been vaccinated with a single dose and this number is rising rapidly. However, due to the emerging variants of COVID-19, the efficacy of the majority of vaccines is decreasing. So, the manufacturers must work on making the vaccines more effective against these new variants as well. This review is written with the intention of summing up all the reported data regarding AZD1222 in order to provide a proper overview

1. Introduction

The year 2019 AD ended up with the inception of a potentially lethal and contagious viral infection reported to be caused by SARS-CoV-2 (Severe Acute Respiratory Syndrome, Coronavirus Type 2). It was declared as the cause of a pandemic on 11th March, 2020 [1]. Since the day the genome of SARS-CoV-2 was discovered, scientists all over the world have been busy in the search of its modes of treatment and prevention [2]. The development of a vaccine is the most effective way to prevent the dissemination of SARS-CoV-2 [3]. Spike (S) protein encoding gene is the major hit point for

vaccine development [3]. SARS-CoV-2 genome has the potential of accumulating plenty of mutations, as it has a RNA-based genome devoid of code reading ability [4]. Receptor binding domain (RBD) of S1 subunit has been proved as the mutational hotspot. Until now, about 1800 mutations have been reported in Spike (S) protein, out of which 235 are dominating in RBD [5]. Various types of vaccines are under investigation, such as subunit vaccines, viral vector-based vaccines, protein-based vaccines, and DNA- and mRNA-based vaccines. More than 180 vaccine candidates are under development, many of these are in clinical trials exhibiting varying effectiveness [6]. The genome of the SARS-CoV-2 is RNA and it is more prone to aquire mutations. This is because RNA polymerases do not have any proofreading ability. Many variants of SARS-CoV-2 have been reported, some of them are variants of interest (VOI) and others are variants of concern (VOC) [3, 7]. The emergence of new variants is the reason due to which the effectiveness of various vaccines is decreasing [8]. Azd1222 (ChAdOx-1) is one of the vaccines developed by AstraZeneca and Oxford University working in collaboration. It is an adenoviral vector-based vaccine and it exhibited 63% efficacy [9]. It also exhibited some side effects as well. Its background, formulation, mode of action, immune responses, clinical trials, and side effects are discussed in this review.

2. AstraZeneca

"AstraZeneca plc" is enlisted as a British-Swedish pharmaceutical organization with its work activities orchestrated in two regions: Gothenburg (research center) and Södertälje (production center) [10]. The company "AstraZeneca" was established via the union of Astra AB of Sweden and the Zeneca Group of London. Now, it is well-known all over the world for producing therapeutics to combat diseases. These days, this company is in the spotlight because of its contribution in the fight against the deadly COVID-19 pandemic, that is, because of the vaccine it has developed to combat SARS-CoV-2 [11]. AstraZeneca, in collaboration with the Oxford University, developed the COVID-19 vaccine named AZD1222, Covishield or Vaxzevria, that belongs to the category of viral vector-based vaccines [9].

3. Viral Vector-based Vaccines

Viral vectors are mostly exploited by molecular biologists to carry the desired genetic material into the cells. Scientifically, this process is known as transduction and such cells are known as transduced cells [12]. Viral vectors possess the capability of being used for gene therapy as well as for the development of vaccines [13]. Adenovirus and vaccinia virus are the most widely used viruses, other than them there are many other viral vectors (presented in Table 1) with their respective advantages and disadvantages [14].

Depending on the potential of the respective virus to infect different types of cells, viral vectors are considered as efficient tools for "vaccines" and "gene therapy" [15, 16]. There are several reasons due to which viral vectors are exploited by biologists. Firstly, they possess extremely specific gene delivery into the targeted cells. Secondly, they efficiently undergo gene transduction. Thirdly (and most importantly), they possess the ability to induce a robust immune response and elevate cell mediated immunity [14]. Viral vector vaccines are better than subunit vaccines because they can generate CTL response due to intracellular expression of

antigens [17]. To produce viral vector-based vaccines scientists opt for the last pathogenic virus candidate, otherwise the implementation of genetic engineering can diminish the pathogenicity of the selected viruses. Furthermore, their ability to replicate their genome is disabled. For example, in adenovirus-based vectors the E1A and E1B encoding regions, which are needed for replication in infected cells, are deleted and replaced with the target gene [14].

4. Viral Vector-based Vaccines for SARS-CoV-2

In order to prevent the infection caused by the potentially lethal SARS-CoV-2 virus, about 22 viral vector-based vaccine candidates have been reported until recently. Out of these 22 viral vector-based vaccines, the majority comprises non-replicating vaccines. On the other hand, there are a few replicating viral vector vaccines, viral vector + APC, and non-replicating viral vector + APC vaccines available as well [18] (data is presented in Table 2 and Table 3). Viral vector-based vaccines that are in Phase III of clinical trials showed significant results. Out of 63 vaccine candidates that are in the process of development in human clinical trials, about 13 are in Phase III. Of these 13, 4 are replication defective viral vector vaccines. Their effects and side effects are enlisted in Table 4 [19].

Table 1. Viral Vectors along with their Advantages and Disadvantages [14]

Virus	Advantages	Disadvantages
Retrovirus	Long-term gene expression	Generation of replication-competent virus Potential for tumorigenesis Infects dividing cells only
Lentivirus	Long-term gene expression Infects non-dividing and dividing cells	Generation of replication-competent virus Potential for tumorigenesis
Vaccinia virus	High immunogenicity Safety: used as a smallpox vaccine High titer production	Pre-existing immunity
Adenovirus	High immunogenicity Safety: used in many clinic trails High titer production	Pre-existing immunity
Adeno-associated virus	Long-term gene expression Non-pathogenic virus	Low titer production
Cytomegalovirus	Induces a unique CTL response Protects against SIV infection in an animal model	Pre-existing immunity Risk of pathogenesis in specific individuals
Sendai virus	High immunogenicity	Pre-existing immunity

Table 2. Viral Vector-based Vaccine Candidates in Clinical Testing Phase [18]

[Accessed in September 10, 2021]

Platform	Candidate vaccines	No.	Percentage
VVnr	Viral vector (Non-replicating)	17	77.27%
VVr	Viral vector (Replicating)	2	9%
VVr + APC	VVr + Antigen presenting cell	2	9%
VVnr + APC	VVnr + Antigen presenting cell	1	4.5%

Table 3. Viral Vector-based Vaccines in Clinical Trials [18]

[Accessed in September 10, 2021]

Vaccine	Type of vaccine	No of doses	Route	Schedule	Developers	Clinical trial phases
VVnr	chADOx1-S-(AZD1222)	2	IM	Day 0+28	Astrazeneca+Oxford university	Phase 4
VVnr	Recombinant novel coronavirus vaccine (AD5nCov)	1	IM	Day 0	CanSino Biological Inc./ Beijing Institute of Biotechnology	Phase 4
VVnr	AD26.COV2.S	1-2	IM	Day 0 or Day 0+ 5	Janssen Pharmaceutical Johnson & Johnson	Phase 4
VVnr	GRAd-COV2 (Replication defective simian Adenovirus)	1	IM	Day 0	Reithera + Leukocare + Univercells	Phase 2/3
VVnr	VXA-CoV2-1Ad5 Adjuvanted oral vaccine	2	Oral	Day 0 + Day 28	Vaxart	Phase 1
VVnr	MVA-SARS-2-S	2	IM	Day 0 + Day28	University of Munich	Phase 1
VVr	DelNS1-2019-nCoV-RBD-OPT1	2	IN	Day 0+ Day 28	University of Hong Kong, Xiamen University and Wantai Biological Pharmacy	Phase 2
VVnr	AZD2816: ChADOx platform & based on the beta (B.1.351	2	IM	Day 0 + day 28	Astrazeneca + University of Oxford	Phase 2/3
VVnr	PIV5 vector encoding spike protein	1	IN	Day 0	CyanVac LLC	Phase 1

Vaccine	Type of vaccine	No of doses	Route	Schedule	Developers	Clinical trial phases
VVnr	Modified Vaccinia virus Ankara (MVA) expressing Spike protein gene	2	IM	Day 0 + Day 28	German Centre for infection research	Phase 1/2
VVnr	COVIVAC	2	IM	Day 0 + Day 28	Institute of Vaccines and Medical Biologicals, Vietnam	Phase 1/2
VVnr	SC- Ad6-1	1 or 2	IM	Day 0 +/- 21	Tetherex pharmaceuticals Corporation	Phase 1
VVnr	AdCLD-Cov 119 (Adenovirus vector)	2	IM	Day 0 + Day 28	Biological E limited	Phase 1/2
VVnr	BBV154, Adenoviral vector vaccine	1	IN	Day 0	Bharat Biotech international limited	Phase 1
VVnr	Chimpanzee Adenovirus serotype 68 + self amplifying mRNA expressing spike protein	2 to 3	IM	Day 0 + 14+ 28 or Day 0 + 28 + 56 or Day 0 + 122	Gritstone Oncology	Phase 1
VVnr	Human adenovirus type 5, hAd5 S+N Bivalant vaccine	1-2	SC or oral or SL	Day 0+ 21	ImmunityBio, Inc	Phase 1/2
VVnr	COH04S1 (MVA SARS-2-S)	1-2	IM	Day 0 + 29	City of Hope Medical Centre + National Cancer	Phase 1
VVr	Rvsv SARS CoV 2 Vaccine (IIBR-100)	1	IM	Day 0	Israel institute for biological research	Phase 2/3
VVr + Apc	Dendritic cell vaccine AV-COVID-19	1	IM	Day 0	Aivita Biomedical Inc, National institute of Health Research & Development, Ministry of Health Republic of Indonesia	Phase 2
VVr + APC	Covid-19/ aApc vaccine	3	SC	Day 0 + 14 + 28	Shenzen Geno-Immune Medical Institute	Phase 1
VVnr + APC	LV-SMENP-DC Vaccine	1	SC & IV	Day 0	Shenzen Geno-Immune Medical Institute	Phase 1/2

Key: VVr: viral vector (Replicating), VVnr: Viral vector (non-replicating), APC: Antigen presenting cell, IM: Intramuscular, IN: Intranasal, SC: Subcutaneous, IV: Intravenous, SL: Sublingual

Table 4. Viral Vector Vaccines in Phase III Trials and their Effects and Side Effects

Vaccine candidate	Effects [19]		Side Effects
	Antibody Response	T Cell Response	
Ad5 nCoV	Neutralizing antibodies were produced in 97% of participants	T cell responses observed in 88% of participants	Myalgia, headache, fatigue, chills, fever, pain at the injection site, redness [20]
Azd1222	Neutralizing antibodies were produced in all the participants who received the prime boost regime	T cell responses noted in all the participants	Thrombocytopenia, venous sinus thrombosis, hemianopia, severe headaches, hemiparesis, Lethargy, fatigue, lymph enlargement, muscle aches [21]
Sputnik V/ Gam-Covid –Vac	Neutralizing antibodies were produced in 100% cadidates	CD4+/ CD8+ cell response was observed in all participants	Nasal congestion, anaphylaxis, chills, malaise, joint pain, seizures, sore throat, fever, anorexia [21, 22]
Ad26 CoV.2S/ JNJ 78436735	Neutralizing antibodies were produced in 92% participants	CD4+ T cell responses in 80% candidates (Th1 skewed phenotype/ Robust CD8+ cell response)	Headaches, chills, fatigue, fever, pain at site of injection [23]

5. Adenovirus-based Vectors

Adenoviruses are categorized as DNA-based viruses that are double stranded and non-enveloped. They are well-known for causing respiratory and ocular infections. Approximately, 150 adenoviruses are known to exist. Many of these viruses are modified by scientists for vaccine development [24, 25]. On average, an adenovirus has a genome of 40 Kilobaspairs, with 50 genes flanked by 5 and 3 prime LTR regions [26]. The structure and genes of an adenovirus are shown in Figure 2. During the formulation of adenoviral vectors, genes responsible for virus replication are replaced with the gene of interest. In most cases, the E1 and E3 genes are removed [27, 28]. The E1 gene has two further transcripts known as “E1A and E1B”. They are responsible for rendering susceptibility to host cells for virus replication. Secondly, E3 is the host immuno- modulatory gene [29].

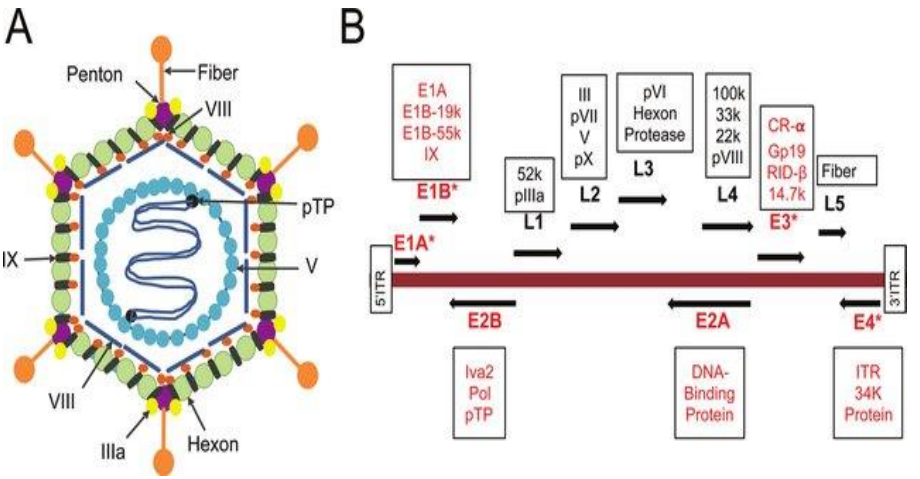

Figure 1. (A) It depicts the structure of the virus and its associated proteins. (B) Genes present in the adenovirus genome, that is, the early genes (E) and the late genes (L). The (*) sign against certain gene names depicts that these genes are mostly deleted in adenovirus vectors [30].

6. Formulation of ChAdOx1 (AstraZeneca Oxford COVID-19 Vaccine)

Visual observation of the SARS-CoV-2 virus particle illustrates the clear visibility of assorted proteins on the exterior of the virus that exhibit a crown-like structure. These proteins are spike proteins, important for entering into the susceptible and permissive host cell. Spike proteins constitute the hotspot region for making the vaccine, as shown in Figure 2 [2].

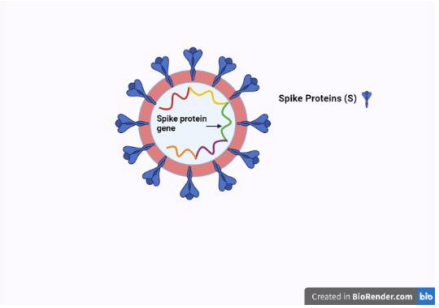

Figure 2. Structure of the SARS-CoV-2 Virus Showing the Spike Protein and its Encoding Gene

The viral vector exploited for forming the ChAdOx1 (Covishield) vaccine was an adenovirus vector obtained from a chimpanzee. Hence, known as the Chimpanzee Adenovirus (ChAd). Its serotype was “Y25” [31] and its genome sequence was sequenced with Accession no JN254802. Serotype Y25 was modified by implementing the genetic engineering approach known as “lambda red recombination” that resulted in the exchange of HAdV-C5’s native genes E4, ORF6, ORF6 and ORF6/7 to form the ChAdOx-1 [32, 33].The pictorial flow chart depicting the formation of ChAdOx-1 vector vaccine is shown in Figure 3.

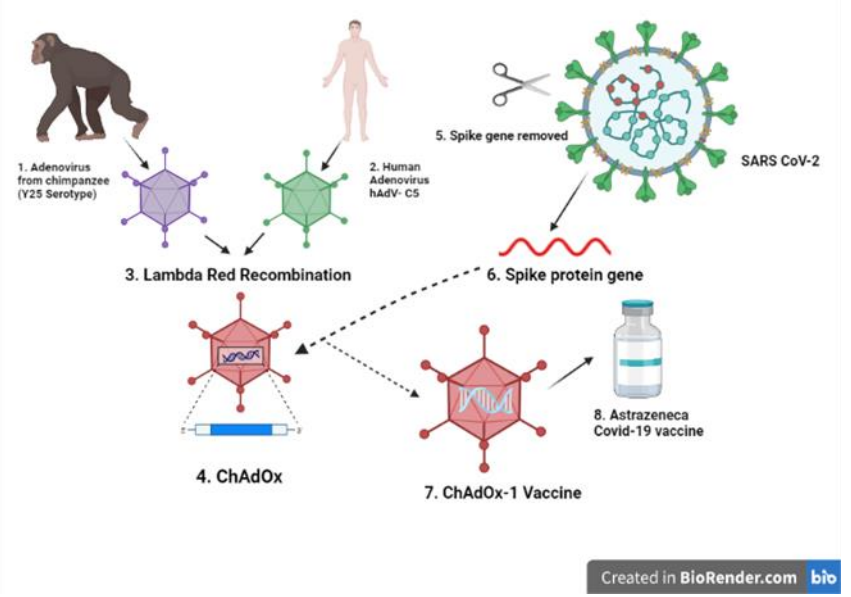

Figure 3. Steps involved in the formation of an adenovirus based vaccine (ChAdOx-1 / Azd1222).

Two serotypes of the adenovirus were taken from a chimpanzee and a human subject: Y25 and hAdV-C5. Lambda red recombination was performed that resulted in the formation of a recombinant adenovirus serotype labeled as ChAdOx. Further, the spike protein gene of SARS-CoV-2 was inserted into it. This final recombinant adenovirus vector was labeled as ChAdOx-1 and it is basically the AstraZeneca Oxford COVID-19 vaccine.

7. Composition of AZD1222 Vaccine

The volume of one dose is 0.5 ml (500ul). Each dose comprises 2.5×10^8 infectious units. In total, 2 doses of vaccine are administrated, intermuscularly. This vaccine was produced using the HEK-293 cell line, which is an altered human embryonic kidney cell line [34]. The other components added to it for stabilization purpose are mentioned below in Table 5.

Table 5. Components Added into ChAdOx-1/Azd1222 Vaccine for Stabilization [34]

No.	Ingredients
1	L- Histidine
2	L- Histidine HCl Monohydrate
3	Magnesium chloride. $6H_2O$
4	Polysorbate 80 (E 433),
5	Sucrose
6	Disodium edetate. $2H_2O$
7	Water

8. Mode of Action

The adenovirus vector holds potent information regarding the formation of Spike protein in the host cell. Unlike the mRNA-based vaccines, AZD1222 is a DNA-based vaccine. This virus has the potential of entering into the host cell but it lacks the ability to replicate itself. In comparison with the mRNA-based

vaccines, AZD1222 owns a stable DS DNA and also enjoys the protection of the adenoviral coat [35], as shown in Figure 4.

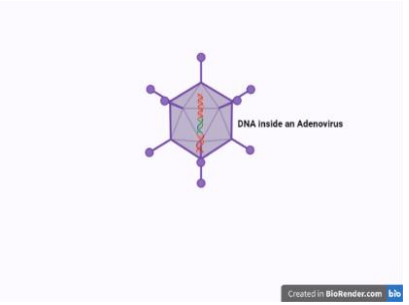

Figure 4. Adenovirus Enclosing the DS DNA (Double Stranded Deoxyribonucliec Acid)

This vaccine is administrated intramuscularly into the deltoid muscle of the arm [36]. Firstly, the virus lodges onto the host cell via its surface proteins. Reciprocally, the cell engulfs the virus in the bubble and after the bubble housing the virus enters into the cell, the virus moves towards the nucleus and transfers its DNA in the nucleus. Here, the Spike protein encoding gene becomes readable by the cell and generates the mRNA [36], as depicted in Figure 5.1.

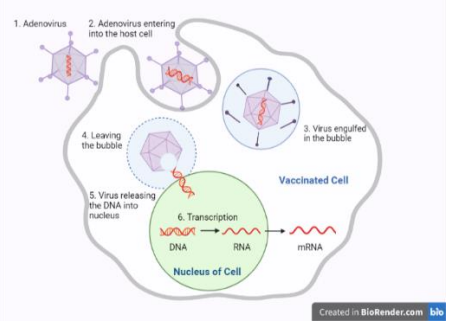

Figure 5.1. Entry of the adenoviral vector vaccine into the cell. With the help of the viral surface proteins, the virus lands onto the cell and then enters into the cell engulfed in a bubble that is eventually disrupted when it reaches the nuclear membrane. Here, the virus releases the genome into the nucleus and then DS DNA undergoes transcription, resulting in the formation of mRNA.

After the formation of mRNA, it is delivered into the cytoplasm where the translation of the Spike gene is carried out. It results in the formation of spike proteins after sophisticated assembly. Some of the spike proteins are distorted into small spike fragments as well. Spike proteins and spike fragments move to the cell surface and protrude out of the host cell. Moreover, they are presented by the host cell for further immune response [35], as depicted in Figure 5.2.

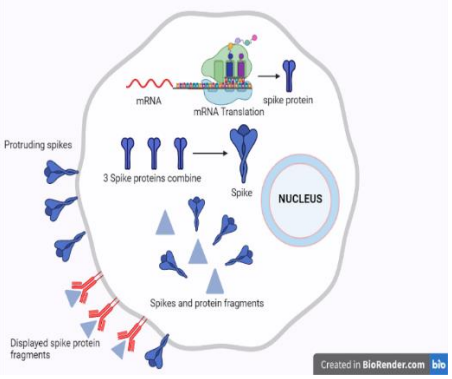

Figure 5.2. Formation of spike proteins and their presentation on the cell surface. After transcription, mRNA is released into the cytoplasm where translation starts and spike proteins are formed. Instead of spike proteins, some spike fragments are also formed that are displayed on the cell surface.

9. Immune Responses

The translated spike proteins are recognized as foreign agents by the cell itself. As a reaction, the cells alarm system

is turned on and a strong immune response is generated. Whenever the vaccinated cell dies, spike proteins and spike fragments are present in the cell debris. The antigen presenting cells (macrophages) pick up these proteins and after digesting them, protein fragments are presented on their surface. Helper T cells are recruited at the surface where these cells detect the presented proteins and aid other cells of the immune system to put themselves in the tussle against diminishing the infection [35, 37], as depicted in Figure 6.1.

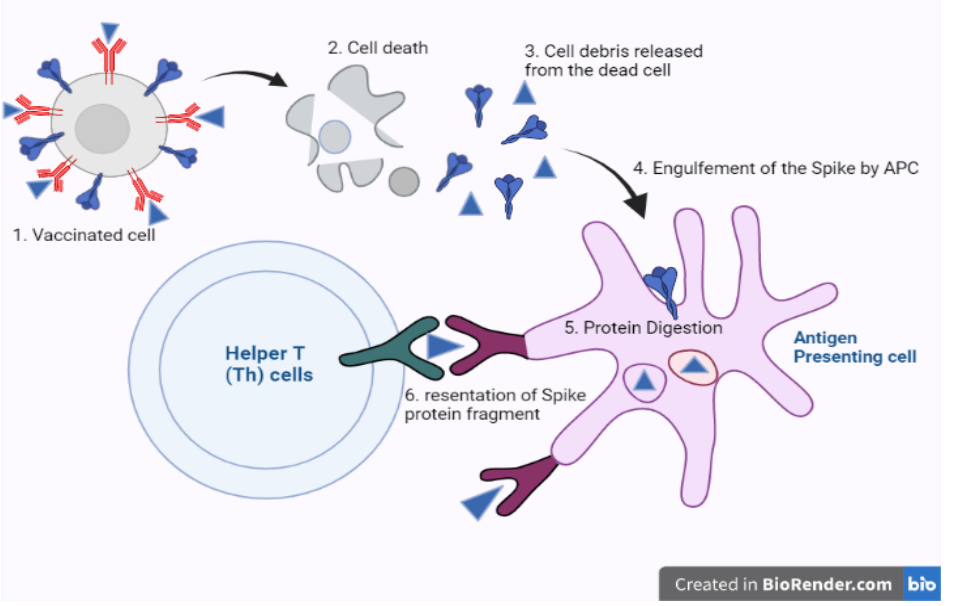

Figure 6.1. Engulfment of the Spike protein by APC (antigen presenting cell) and recruitment of (Th) Helper T cells. The spike proteins present in the cell debris are engulfed by the APC. After protein (spike protein) digestion, spike protein fragments are presented on the surface of APC that further recruits the (Th) Helper T cells.

Another type of immune cells known as the B cells lodge themselves onto the spike proteins residing on the vaccinated cell or on the freely available spike fragments. The B cells are activated when they come in contact with the Helper T cells. After activation, the B cells undergo proliferation (clonal expansion). This results in the formation of plasma cells and the Memory B cells. Plasma cells form the antibodies, fight with the invaders, and start diminishing the infection. On the other hand, Memory B cells are there for controlling the infection in the future (Figure 6.2). The antibodies produced by plasma cells attach to the spike proteins of the virus and prevent them from attaching to other cells. In this way, the antibodies protect the uninfected body cells (Figure 6.3) [35, 37, 38, 39].

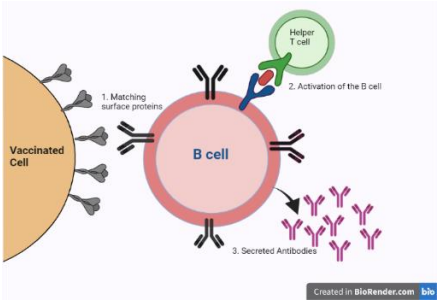

Figure 6.2. Activation of the B cells and the release of antibodies. The spike proteins presented on the vaccinated cell are detected by the B cells which are activated when they come in contact with the (Th) Helper T cells. The activated B cells undergo proliferation and release antibodies that fight to remove the infection.

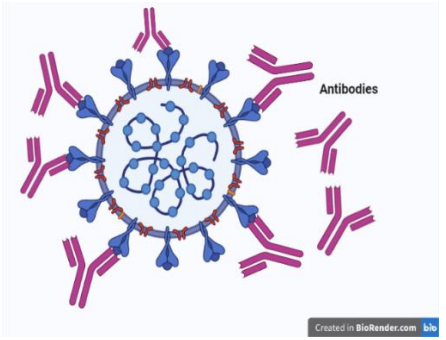

Figure 6.3. Antibodies released from the plasma B cells attached with the spike proteins of the virus, preventing it from attacking the body cells.

On the other hand, APC has the ability to activate the Killer T cells (CTL). These cells have the potential to kill the COVID-19 infected cells that exhibit the spike protein fragments on them, as shown in Figure 6.4 [35, 40].

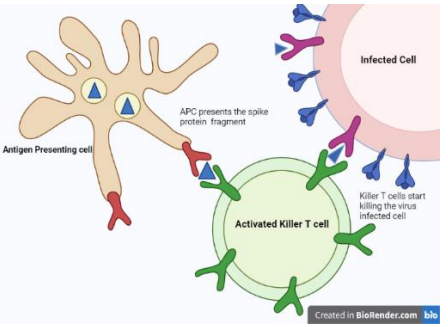

Figure 6.4. APC activates the Killer T cells. The activated Killer T cells kill the virus infected cell.

10. Clinical Trials and Approval

Back in the July of 2020, in collaboration between IQVI and AstraZeneca, clinical trials were planned and initiated in the US [41]. In early September of 2020, clinical trials were paused, reportedly due to the adverse effects of the vaccine. Afterwards, trials were reinitiated when safety was assured by the developers [42, 43]. By the end of 2020, Oxford University revealed the results of the ongoing trials (Phase III), according to which ChAdOx-1 exhibited 70% efficacy [44, 45, 46]. In February 2021, 76% efficacy of ChAdOx-1 was reported and the drug was able to prevent symptomatic COVID-19. On the other hand, a single dose had no against asymptomatic COVID-19 [47]. The results of clinical trials conducted in the USA reported that this vaccine can prevent 79% of subjects from symptomatic COVID-19 [48].

By the end of March 2021, Oxford University decided to initiate the intranasal spray vaccine trial (Phase 1) [49]. UK was one of the first countries which allowed short-term emergency use of AstraZeneca vaccine [50]. EMA recommended the authorization for its administration on subjects who were 18 years of age or above

on 29th January, 2021 [51]. ChAdOx1 nCoV-19 has been authorized by many countries for emergency administration but it has not been approved by the Food and Drug Administration (FDA) yet [35]. Figures 7.1 and 7.2 depict the countries that have approved the use of adenovirus vector-based vaccines. While, the reported side effects of the ChAdOx-1 vaccine are enlisted in Table 6.

Table 6. Side Effects of ChAdOx-1/ Azd1222 Vaccine [Accessed in 17th September, 2021]

Side Effects (1 in 10 people)	Side Effects (1 in 100 people)	Side Effects (1 in 100,000 people)	Other Rare Side Effects
Vomiting, fever, diarrhoea, swelling, low level of platelets[3]	Decreased appetite, dizziness, sweating, sleepiness, itching, rashes, abdominal pain, enlarged lymph nodes[3]	Blood clots + low level of platelets, thromboembolic events[4,5]	Anaphylaxis, capillary leak syndrome, Guillain-Barré syndrome[6,7]

[3https://www.ema.europa.eu/en/medicines/human/EPAR/vaxzevria-previously-covid-19-vaccine-astrazeneca]
[4https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1018448/Coronavirus_vaccine_-_summary_of_Yellow_Card_reporting_08.09.2021_-_Cleared_Final.pdf]

[5https://www.ema.europa.eu/en/news/astrazenecas-covid-19-vaccine-benefits-risks-context]

[6https://www.ema.europa.eu/en/news/vaxzevria-ema-advises-against-use-people-history-capillary-leak-syndrome]

[7https://www.ema.europa.eu/en/documents/covid-19-vaccine-safety-update/covid-19-vaccine-safety-update-vaxzevria-previously-covid-19-vaccine-astrazeneca-8-september-2021_en.pdf]

7.1. Approval of Adenovirus Vector-based Vaccines in the World [52] [Accessed on September, 2021]

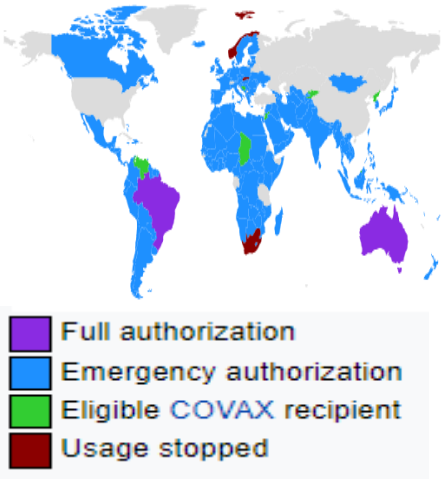

Figure 7.2. Geographical Authorization of Oxford AstraZeneca Vaccine [52] [Accessed in September 14, 2021]

According to the most recent data, about 42.6% of the world has been vaccinated (single dose) and 5.82 billion doses of the vaccine have been administrated all over the world. Figure 7.3 shows the number of the fully vaccinated people, globally [53].

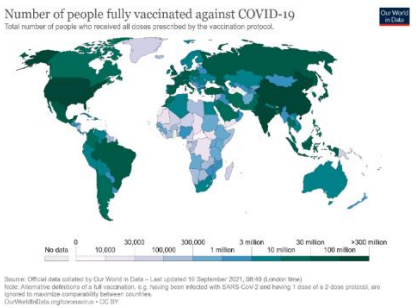

Figure 7.3. Number of the Fully Vaccinated People in the World (Single Dose) [Accessed in 17th September, 2021]

11. Effectiveness of AstraZeneca against SARS-CoV-2 Variants

Emerging variants of SARS-CoV-2 pose a challenge for the world [54]. SARS-CoV-2 accumulates a high rate of mutations, mostly in the Spike gene, which results in the emergence of new variants. Consequently, the efficacy of the vaccine changes accordingly [8]. A vaccine is considerably effective in case the estimation is ≥50%, with a >30% lower limit of the 95% confidence interval. It has been deduced that the effectiveness of a vaccine reduces with the passing of time [55, 56]. The effectiveness of Oxford AstraZeneca vaccine against the Alpha and Delta variants of SARS-CoV-2 is shown in Table 7.

Table 7. Effectiveness of ChAdOx-1/Azd1222 against the SARS-CoV-2 Variants [58]

Doses	Severity of Illness	Alpha Variant	Delta Variant
First	Symptomatic	39%	33%
	Asymptomatic	37%	18%
Second	Symptomatic	81%	61%
	Asymptomatic	73%	60%

It has been dwindling with the passing of time. A study has reported the possible reasons behind its reduced effectiveness. According to it, vaccine effectiveness (VE) is reduced as the rate of vaccination increases. Secondly, it is also reduced due to poor estimation and monitoring of patients because of limited observation time and very low infection ratio in the people [57].

12. Heterologous Prime Boost Vaccination

More than one prime immunization booster doses are required to enhance the effectiveness of any vaccine. Conventionally, shots of the same vaccine are administrated as “homologous boosts”. It has been reported that the prime boosts of immunization can also be administrated

using different vaccines that possess the same antigen. This is known as "heterologous prime boost vaccination" and it can exhibit more immunogenicity then that of the homologous boosts. According to recent researches, HPBV (heterologous prime boost vaccination), comprising Oxford AstraZeneca vaccine + Pfizer BionTech vaccine, generates robust immune responses in the form of high levels of antibodies and T cell activity. On the other hand, a combination of Oxford AstraZeneca + Moderna generates a high level of spike specific CTL response.

13. Neutralizing Antibodies using AZD1222

Wall et al. determined the neutralizing antibodies titre "nAb" using the "High Throughput Live Virus SARS-CoV-2 Neutralization Assay" after either a single or a double dose of AstraZeneca. A broad range of nAbs were generated after a single dose of AstraZeneca. On the other hand, their levels were even higher in candidates with prior SARS-CoV-2 symptoms. In another study, it was revealed that the titres of nAbs were low in AstraZeneca recipients, as compared to the Pfizer recipients.

14. AZD1222 Vaccination Recommendation

A very important question is that who can get vaccinated by AZD1222 and who can't. So, in accordance with the WHO guidelines, people with comorbidities must be vaccinated because they may experience severe illness after getting infected with SARS-CoV-2. Similarly, people who are HIV positive and remain immunocompromised must also be vaccinated after proper counseling and consultation. Breastfeeding women can be vaccinated if they belong to the vaccination prioritized group. Pregnant women can be vaccinated if they are at a risk of getting exposed to the virus or have comorbidities. However, prior consultation with their health care provider is preferable for them.

15. Conclusion

Any vaccine that has approximately 50% efficacy can be considered as an effective candidate to prevent the SARS-CoV-2 mediated infection. The trials, until now, have demonstrated more than 50% efficacy for AZD1222. However, the decreasing efficacy of ChAdOx-1 (Azd1222) against the emerging variants is a point of concern, as the majority of vaccines exhibited diminished efficacy against B1.617 (Delta variant). Secondly, AstraZeneca also entails some side effects that must be considered by the manufacturers. So, ChAdOx-1/Azd122 must have high efficacy and few side effects. Most importantly, its effectiveness should be maintained against the newly emerging variants.

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