Resistance towards ChadOx1 nCoV-19 in an 83 Years Old Woman Experiencing Vaccine Induced Thrombosis with Thrombocytopenia Syndrome

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Methods for Assessing Resistance to Non-Integrating Virus Vectors

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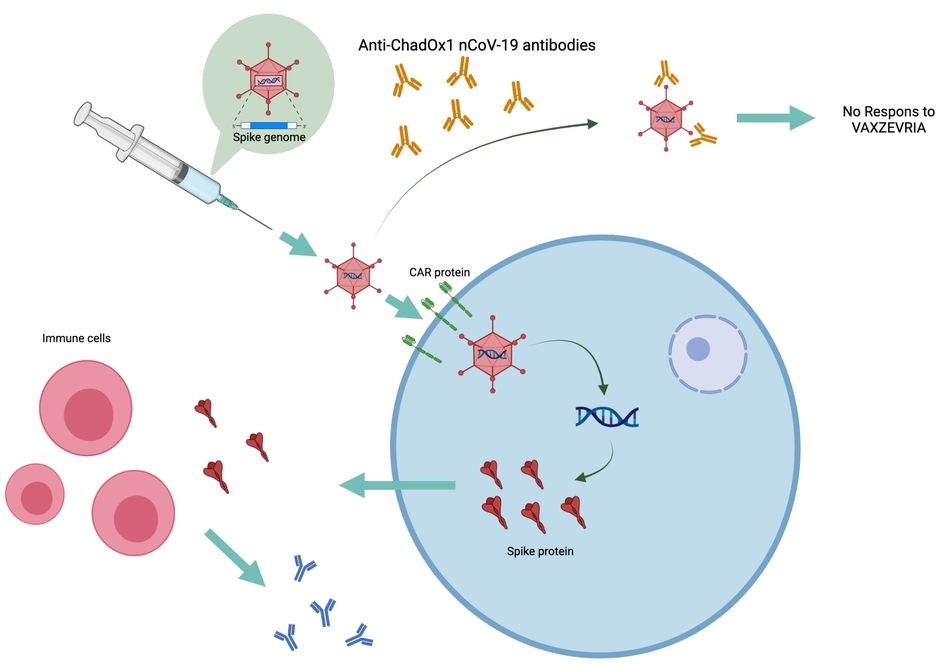
INTRODUCTION

The use of adenoviruses for the development of vaccines has been known for almost 20 years [1]. The use of these viral vectors is ideal for vaccine therapy due to their ability to induce innate immunity and adaptive immunity in the host. In this case-report, we further investigate the case of an 83-year-old woman vaccinated with **ChadOx1 nCoV-19** who developed a vaccine-induced thrombosis with thrombocytopenia syndrome (TTS). Interestingly, on top of her TTS, she did not develop an antibody response against the spike protein of SARS-CoV-2 following the administration of her first dose of ChadOx1 nCoV-19.

METHODS

A **cellular model** for assessing resistance to the ChadOx1 nCoV-19 in the Vaxzevria® vaccine was developed. This test is based on the detection of the production of the spike protein (S protein) induced by ChadOx1 nCoV-19 (lot number: ABW4805) in the supernatant fraction of cells transfected by the adenovirus vector (**Figure 1**).

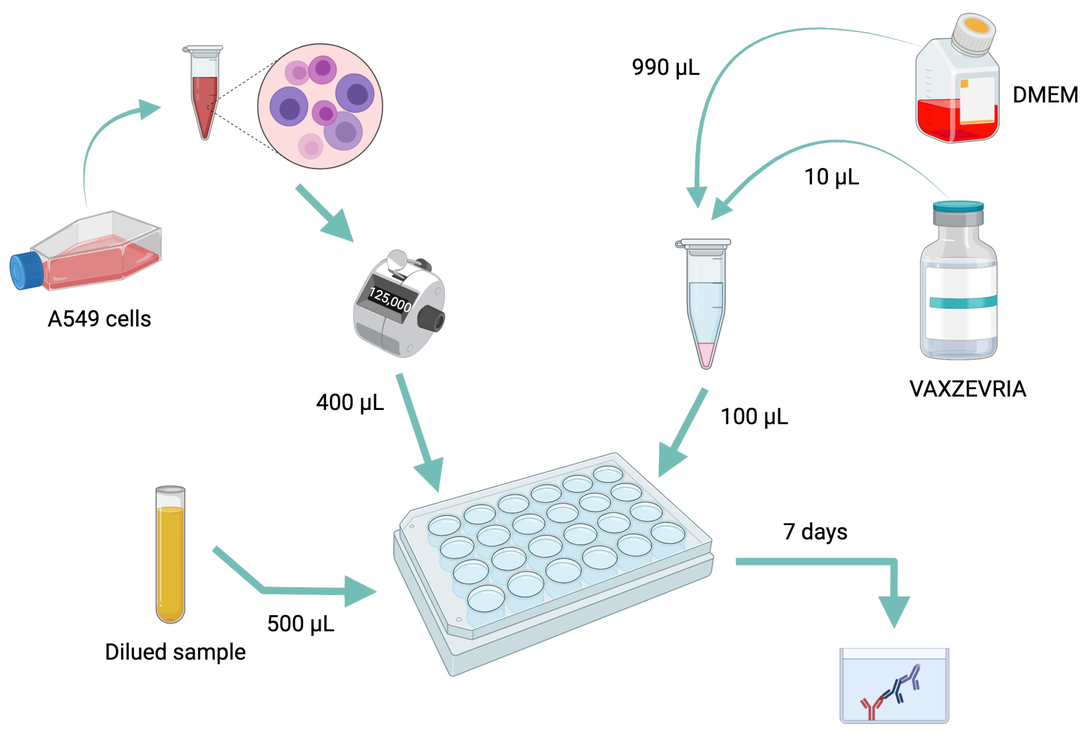
Figure 1



The model is then exposed to the serum of the tested patient.
In presence of elements impairing the infection of the cells by ChadOx1 nCoV-19 as **anti-adenovirus antibodies** or other elements present in the serum to prevent the action of the adenovirus, the production of the S protein in the supernatant is reduced or abolished.

A549 cells (human lung adenocarcinoma cell line) were dispensed into a 24-well plate at an optimal concentration to achieve confluence without excessive cell death. This cell mat was then placed with a fixed amount of ChadOx1 nCoV-19 vaccine and a progressive dilution of the patient's or control's serum.
The plate was then left for 7 days at 37 ˚C and 5% of CO_2 in a calibrated incubator. Measurement of the amount of S protein present in the supernatant after 7 days of incubation was performed using ELISA technique. (**Figure 2**)

Figure 2



RESULTS

The **controls all have positive anti-SARS-CoV-2 S protein antibodies titers** with a mean titer of 2427 AU/mL (95% CI: 1581 AU/mL–6434 AU/mL) and negative anti-NCP antibodies titers. The results for the serum analysis of the patient not responding to Vaxzevria® are presented in **Table 1**.

Table 1

Sample Dilution Factor	Sample D0 Absorbance	Sample D1 Absorbance
1/4	0.07	0.07
1/8	0.07	0.07
1/16	0.06	0.08
1/32	0.06	0.08
1/64	0.06	0.07
1/128	0.08	0.06
1/256	0.07	0.06
1/512	0.08	0.08
1/1024	0.07	0.07

The absorbance does not vary according to the serum dilution and remains between 0.06 and 0.08. These values were below the limit of quantification (LOQ) of the ELISA assay (LLOQ = 2 ng/mL). The results obtained with the controls provide mean concentrations for the different serum dilutions ranging from 21.60 ng/mL (95% CI: 17.20 ng/mL–26.00 ng/mL) to 24.52 ng/mL (95% CI: 17.23 ng/mL–31.81 ng/mL). (**Table 2**)

Table 2

Sample Dilution Factor	VAXZEVRIA Double-Vaccinated Patients Mean Concentration (ng/mL)
1/4	24.52 (95% CI: 17.23–31.81)
1/8	23.36 (95% CI: 17.00–29.71)
1/16	24.28 (95% CI: 17.21–31.35)
1/32	21.98 (95% CI: 14.82–29.13)
1/64	22.71 (95% CI: 14.24–31.19)
1/128	22.81 (95% CI: 16.15–28.99)
1/256	22.57 (95% CI: 16.15–28.99)
1/512	21.60 (95% CI: 17.20–26.00)
1/1024	24.06 (95% CI: 18.16–29.96)
Overall mean (ng/mL)	23.10 (95% CI: 22.31–23.89)

CONCLUSION

Based on the results obtained, it can be assumed that the clinical case presented in this paper developed a form of **resistance against the adenovirus used in the ChadOx1 nCoV-19 vaccine**. The origin of this resistance is still unknown, but this test allows to eliminate a possible lymphocytic or myelocytic origin.
The model developed is applicable to **other therapies** using adenoviruses vector such as anti-cancer therapies or several vaccines already on the market such as Ebola vaccine (Zabdeno®) or other COVID-19 vaccine as the Johnson & Johnson vaccine (Jcovden®).
In addition to these therapies already on the market, several studies are underway to develop a malaria vaccine based on adenoviruses such as Ad35 or Ad26.
The test developed would therefore make it possible to **assess an individual's resistance to an adenovirus-based therapy** more widely. This would make it possible to prevent the use of certain therapies that we know will not work in a particular individual. Importantly, a link with the TTS developed by our patient cannot be excluded and deserved further investigations

CONTACT INFORMATION

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