ENSEMBLE
A COVID-19 STUDY

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Janssen
PHARMACEUTICAL COMPANIES OF
Johnson & Johnson

Janssen ENSEMBLE: VAC31518COV3001

A Randomized, Double-Blind, Placebo-Controlled Phase 3 Study to Assess the Efficacy and safety of Ad26.COV2.S for the Prevention of SARS-CoV-2-mediated COVID-19 in Adults Aged 18 Years and Older

SECTION 2.1

ENSEMBLE Study Rationale

The development of a vaccine for coronavirus disease-19 (COVID-19) will be critical for containing the current outbreak and preventing future outbreaks, as no vaccine is currently available.

Janssen is developing a vaccine for the prevention of SARS-CoV-2-mediated COVID-19 in adults.

SECTION 2

Key Features of the Investigational Vaccine - Ad26.COV2.S

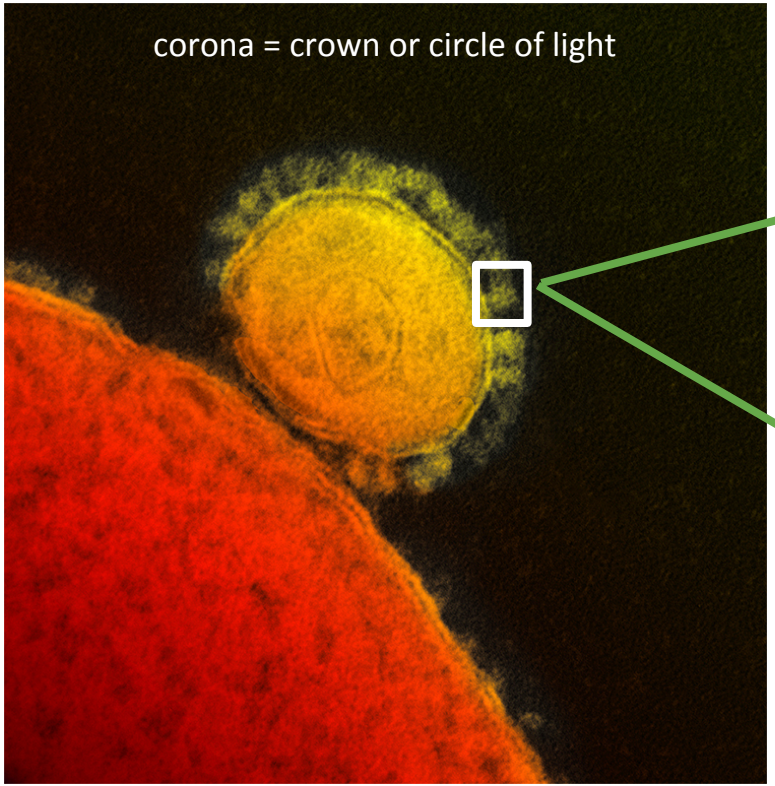
Monovalent

Composed of a recombinant replication-incompetent adenovirus type 26 (Ad26) vector constructed to encode the SARS-CoV-2 S protein, the major surface protein of coronaviruses

Administered as a single-dose ($5x10^{10}$ vp) IM injection

Not yet approved by any regulatory authority

SARS-CoV-2 and its spike protein (the vaccine target)



Slide credit: Vaccine Research Center, NIAID

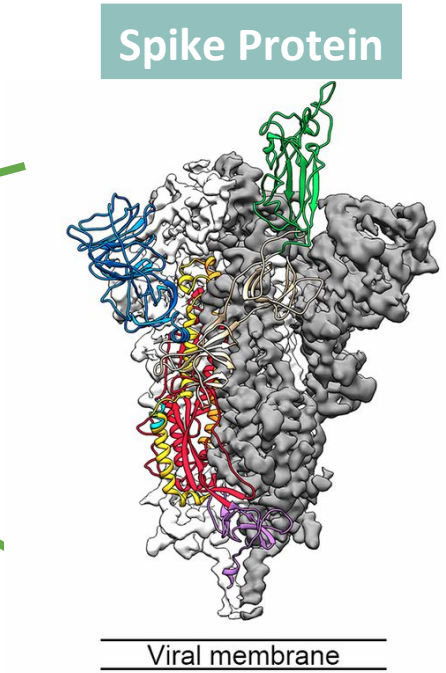


Image credit: Wrapp D, Wang N, Corbett KS, Goldsmith JA, Hsieh CL, Abiona O, Graham BS, McLellan JS. Cryo-EM structure of the 2019-nCoV spike in the prefusion conformation. Science. 2020 Feb 19:eabb2507. doi: 10.1126/science.abb2507.

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The adenovirus vaccine design

- Viral vector vaccine
- 2 main components: adeno virus (vector) + copy of the spike protein (insert)
- The vaccine in this study uses a non-functional version of a type of cold virus called Adenovirus 26 as the vector (like the FedEx delivery truck).
- The Adenovirus has been changed so that it cannot cause you to get a cold.
- The package delivered in the truck, or the insert, is a copy of the spike protein found on the surface of SARS-CoV-2.

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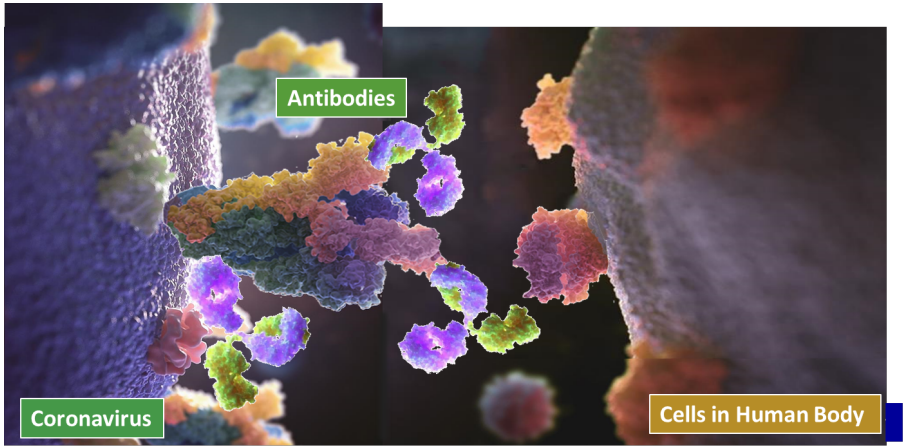
The adenovirus vaccine design

- Adenoviruses are common so need to find one that is rare or use a vector that infects other primates like the CHIMP adeno virus (Astra Zeneca)
- J&J uses an AD26
- Immune response to both the vector and the insert
- They do not interact with our DNA in anyway
- Viral vector vaccines are more stable and don’t have such demanding cold chain requirements



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Study Design

SECTION 1.1

Key Features of the ENSEMBLE Study

Multicenter

Phase

3

Double-Blind

1:1 randomization to Ad26.COV2.S or placebo (0.9% NaCl)

The **efficacy, safety and immunogenicity of Ad26.COV2.S will be assessed in adults** ≥18 to <60 years of age and ≥60 years of age that are in or going to locations with a high risk of SARS-CoV-2 infection.

SECTION 1.3

Study Timeline

Vaccination | Temperature | Blood Draw | Baseline Risk Factor Assessment Questionnaire

2 years and 1 month

Screening

Visit 1
Day -28 to 1

Study Period

Visit 2
Day 1

+ 28 days
Visit 3
Day 29

+ 70 days
Visit 4
Day 71

+ 24 weeks
Visit 5
Week 24

+ 52 weeks
Visit 6
Week 52

Long-Term Follow-Up

+ 78 weeks
Visit 7
Week 78

+ 104 weeks
Visit 8
Week 104

Post-vaccination observation period 30 mins for first 2,000 participants in each age group

May be decreased to 15 mins for the remaining participants if no acute reactions

COVID-19 Signs and Symptoms Surveillance and AE Recording
Symptoms of Infection with Coronavirus-19 questionnaire completed by patients in the e-Diary

SECTION 1.1

Planned Enrollment

Approximately 60,000 adult participants will be enrolled and randomized 1:1 to 1 of 2 groups:

Group 1:
Ad26.COV2.S
($1x10^{11}$ vp)

Group 2:
Placebo
(0.9% NaCl)

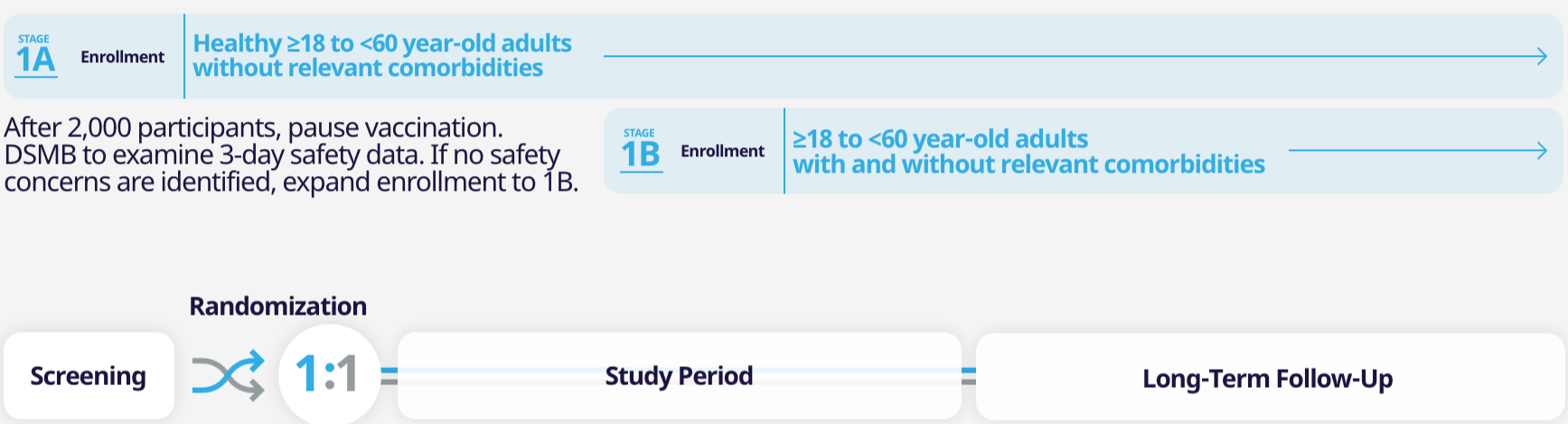
Additional information will be collected for some participants in sub-studies:

Immuno Subset:
400 participants for collecting additional information about immune responses to Ad26.COV2.S

Safety Subset:
6,000 participants for collection of additional information on solicited and unsolicited Adverse Events

SECTION 1.1

Study Design: Staggered Enrollment Stage 1



SECTION 1.1

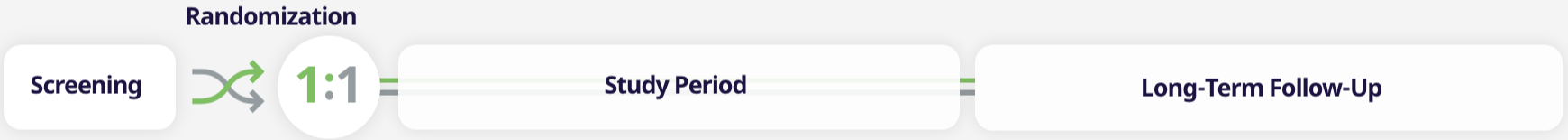
Study Design: Staggered Enrollment Stage 2

STAGE 2A Enrollment — Healthy ≥60 year-old adults without relevant comorbidities

Goal to enroll a minimum of ~ 30% of study population →

After 2,000 participants, pause vaccination. DSMB to examine 3-day safety data. If no safety concerns are identified, expand enrollment to 2B.

STAGE 2B Enrollment — ≥60 year-old adults with and without relevant comorbidities →



Stage 2a will run in parallel with Stage 1a unless not allowed per local Health Authority guidance.

Study Objectives and Endpoints

SECTION 1.1

Overview

In this study, efficacy, safety and immunogenicity will be evaluated in adults living in or going to locations with high risk of **SARS-CoV-2** infection after vaccine administration

Defining COVID-19:

- Molecularly confirmed **COVID-19** is defined as a positive **SARS-CoV-2** viral RNA result using a PCR-based or other molecular diagnostic test
- Severity of all **COVID-19** cases will be assessed independently by a clinical evaluation committee (CEC)

SECTION 3

Primary Objective and Endpoint

Objective

To demonstrate the efficacy of Ad26.COV2.S in the prevention of molecularly confirmed, moderate to severe/critical COVID-19, as compared to placebo, in SARS-CoV-2 seronegative adults

Endpoint

First occurrence of molecularly confirmed, moderate to severe/critical COVID-19, with onset at least 14 days post-vaccination (Day 15)

Secondary Objectives – Efficacy (1/2)

- Prevention of molecularly confirmed, **moderate to severe/critical** COVID-19, as compared to placebo, in adults **regardless of their serostatus**
- Efficacy of Ad26.COV2.S in the prevention of molecularly confirmed, **moderate to severe/critical** COVID-19 in SARS-CoV-2 **seronegative** adults, as compared to placebo, with onset 1 day after study vaccination
- Effect of Ad26.COV2.S on COVID-19 requiring **medical intervention** (based on objective criteria) compared to placebo
- Effect of Ad26.COV2.S on SARS-CoV-2 **viral RNA load** compared to placebo for moderate to severe/critical COVID-19

Secondary Objectives – Efficacy (2/2)

- Effect of Ad26.COV2.S on molecularly confirmed **mild** COVID-19
- Effect of Ad26.COV2.S on COVID-19 as defined by the US **FDA harmonized case definition**
- Effect of Ad26.COV2.S on all molecularly confirmed **symptomatic** COVID-19, as compared to placebo
- Effect of Ad26.COV2.S on occurrence of **asymptomatic** or undetected infections with SARS-CoV-2, as compared to placebo

Inclusion and Exclusion Criteria

SECTION 5.1

Inclusion Criteria (1/2)

- **Participant must provide consent themselves** (sign consent)
  - Legal representatives cannot provide informed consent
- Participant is **willing to adhere** to prohibitions and restrictions
- **Stage 1a and 1b:** Participant is ≥**18 to <60 years of age** on the day of signing the ICF
- **Stage 2a and 2b:** Participant is **≥60 years of age** on the day of signing the ICF
- **Stage 1a and 2a:** In the investigator's clinical judgement, participant must be either in good or stable health, including a **BMI <30 kg/m²**
- **Stage 1b and 2b:** Participant may have a **stable and well-controlled comorbidity** associated with an increased risk of progression to severe COVID-19

SECTION 5.1

Inclusion Criteria (2/2)

- Before randomization, **female participants must be either**:
  - **Not of childbearing potential** or
  - Of childbearing potential and **practicing an acceptable effective method of contraception** and agrees to remain on such a method of contraception from providing consent until 3 months after administration of study vaccine
- **All participants of childbearing potential must have a negative highly sensitive urine pregnancy test** at screening and on the day of and prior to study vaccine administration
- **Breastfeeding women are allowed for inclusion**
- **Participants that abuse drugs or alcohol are allowed for inclusion**

SECTION 5.2

Exclusion Criteria (1/4)

- Clinically significant acute illness or temperature ≥38.0°C (100.4°F) within 24 hours prior to the planned study vaccination

- Abnormal function of the immune system resulting from:
  - A. Clinical conditions expected to have an impact on the immune response to the study vaccine (e.g. autoimmune disease, potential immune mediated disease or known or suspected immunodeficiency, chronic kidney disease [with dialysis])
  - B. Chronic (>10 days) or recurrent use of systemic corticosteroids within 6 months before administration of study vaccine and during the study
  - C. Administration of antineoplastic and immunomodulating agents or radiotherapy within 6 months before administration of study vaccine and during the study

SECTION 5.2

Exclusion Criteria (2/4)

- **Treatment with Ig** in the 3 months or blood products in the 4 months before the planned administration of the study vaccine
- Participant **received or plans to receive:**
  - A. **Licensed live attenuated vaccines** - within 28 days before or after planned administration of study vaccine
  - B. Other **licensed (not live) vaccines** - within 14 days before or after planned administration of study vaccine
- Previously received a **coronavirus vaccine**
- Received an **investigational drug** (including investigational drugs for prophylaxis of COVID-19) **or used an invasive investigational medical device within 30 days or received an investigational vaccine within 6 months** before the planned administration of the study vaccine or is currently enrolled or plans to participate in another investigational study during the course of this study

SECTION 5.2

Exclusion Criteria (4/4)

- **Cannot communicate reliably** with the investigator
- **Unlikely to adhere to the requirements** of the study, or is unlikely to complete the full course of vaccination and observation
- **Stages 1a and 2a:**
  - A. **Comorbidities that are or might be associated with an increased risk of progression to severe COVID-19**
  - B. **History of malignancy within 1 year before screening**
  - C. **History of acute polyneuropathy** (e.g., Guillain-Barré syndrome)
  - D. **Had surgery requiring hospitalization** within 12 weeks before vaccination, or will not have fully recovered from surgery requiring hospitalization, or has surgery requiring hospitalization planned during the time the participant is expected to participate in the study or within 6 months after study vaccine administration
  - E. Participants with **moderate to severe high blood pressure/hypertension**

COVID-19 Case Management

SECTION 8.1.2

Surveillance for COVID–19-like Signs and Symptoms

All participants will be routinely surveyed for any new symptoms or health concerns that could be related to infection with SARS-CoV-2 **through the e-Diary in Study Hub:**

Vaccination/Randomization visit in Office

Participant trained on device and completion requirements

Year 1

e-Diaries to be completed twice a week

Year 2

e-Diaries to be completed once every 2 weeks starting 1 year after vaccination or after primary analysis (whichever is last) through long-term follow-up

SECTION 9.1

Timing of Planned Analyses

The study will have 3 timepoints for analysis:

1 Primary efficacy analyses to evaluate the primary and secondary objectives

- When target number of events is reached or earlier based on sequential monitoring
- Sponsor will be unblinded, but investigator and participants remain blinded until study completion

2 Final analysis

- When the last participant completes the visit 12 months post-vaccination or discontinues

3 End-of-study analysis

- When all participants have completed the visit 24 months post-vaccination or have discontinued

Study Timelines

- 18th Sep : FDA gives greenlight to start
- 21st Sep: First participant vaccinated in the US
- 6th of Oct: First participant vaccinated in S. America
- 6th Nov: First participant vaccinated in RSA

Enrolment closed for South Africa and South America on the 9th of December.

South African sites recruited ~ 6600 participants in 1 month !

Protocol was amended mid recruitment to decrease sample size.

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Thank You

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