
AstraZeneca
AstraZeneca COVID-19 Vaccine (AZD1222)
National Adult and Influenza Immunization Summit
COVID19 Vaccines Webinar Part 3
Lisa Glasser, MD
US Medical Affairs, Head Vaccines-Infectious Disease
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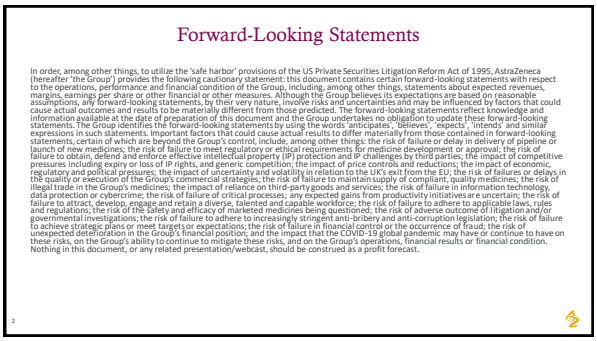
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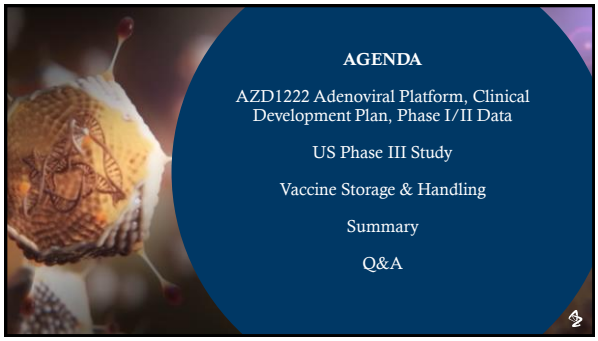
AGENDA
AZD1222 Adenoviral Platform, Clinical Development Plan, Phase I/II Data
US Phase III Study
Vaccine Storage & Handling
Summary
Q&A

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AZD1222 Adenoviral Platform Clinical Development Plan & Phase I/II Data

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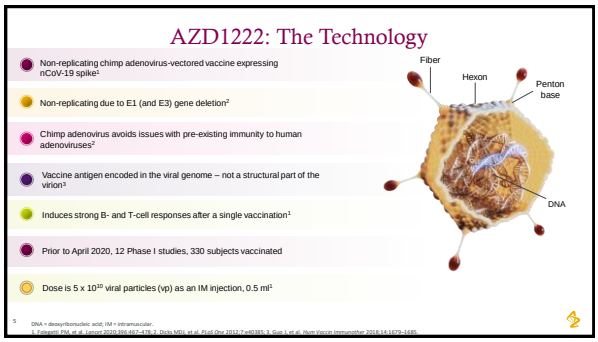
AZD1222: The Technology
Non-replicating chimp adenovirus-vectored vaccine expressing nCoV-19 spike[1]
Non-replicating due to E1 (and E3) gene deletion[2]
Chimp adenovirus avoids issues with pre-existing immunity to human adenoviruses[2]
Vaccine antigen encoded in the viral genome – not a structural part of the virion[2]
Induces strong B- and T-cell responses after a single vaccination[1]
Prior to April 2020, 12 Phase I studies, 330 subjects vaccinated
Dose is 5 x 10^10 viral particles (vp) as an IM injection, 0.5 ml[1]
Fiber
Hexon
Penton base
DNA
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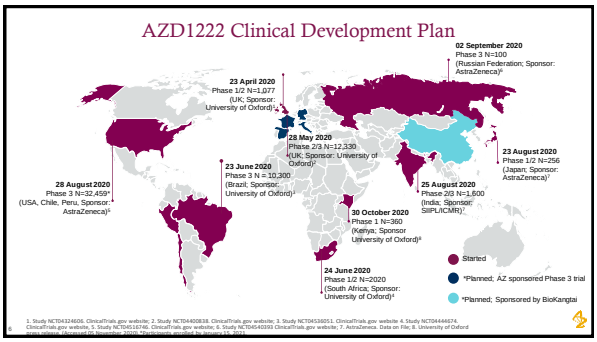
AZD1222 Clinical Development Plan
02 September 2020
Phase 3 N=100
(Russian Federation; Sponsor: AstraZeneca)[2]
23 April 2020
Phase 1/2 N=1,077
(UK; Sponsor: University of Oxford)[3]
28 May 2020
Phase 2/3 N=12,330
(UK; Sponsor: University of Oxford)[3]
23 August 2020
Phase 1/2 N=256
(Japan; Sponsor: AstraZeneca)[3]
23 June 2020
Phase 3 N = 10,300
(Brazil; Sponsor: University of Oxford)[4]
28 August 2020
Phase 3 N=32,459[4]
(USA, Chile, Peru, Sponsor: AstraZeneca)[5]
25 August 2020
Phase 2/3 N=1,600
(India; Sponsor: SIIPL/ICMR)[3]
30 October 2020
Phase 1 N=360
(Kenya; Sponsor University of Oxford)[4]
24 June 2020
Phase 1/2 N=2020
(South Africa; Sponsor: University of Oxford)[4]
Started
*Planned; AZ sponsored Phase 3 trial
*Planned; Sponsored by BioKangtai
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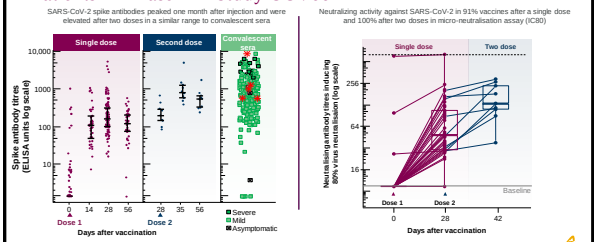
AZD1222 Induced Robust Antibody Responses At Levels In A Similar Range To Those Seen In Convalescent COVID-19 Patients In Phase I/II Study COV001



Folegatti P et al. *The Lancet*. 2020.

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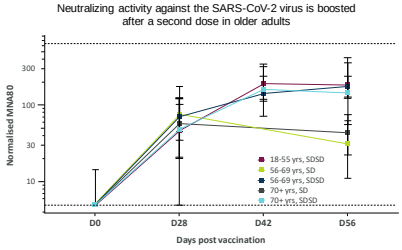
Robust Humoral Response In Older Adults Receiving AZD1222 In COV002



Ramasamy M et al. *Lancet*. 2020.

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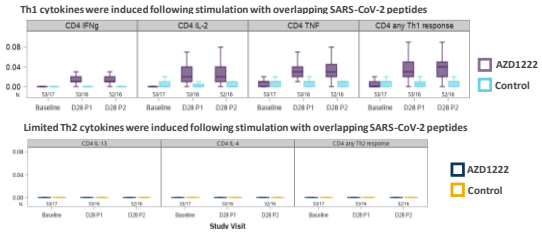
AZD1222 Induced A Robust Th1 Biased T-Cell Response In COV001 And COV002 Participants



D28 P1 = Day 28 post 1st Dose, D28 P2 = Day 28 post 2nd Dose. Boxplots display the median and 1st and 3rd quantiles. Th1 data result indicates percentage of CD69+ cells expressing IFNg, IL-2, TNFα (or any Th1 cytokine) after stimulation with SARS-CoV-2 S1 peptide pool (similar results were seen with S2 peptide pool). Th2 data result indicates percentage of CD69+ cells expressing IL-4, IL-13 (or either Th2 cytokine). Background percentage was subtracted from the stimulated percentage prior to analysis. Stimulated percentages less than the background percentage were set to 0%.

Exploratory analysis, Unpublished results

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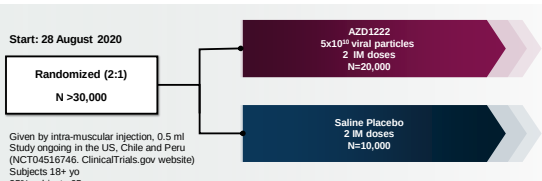
Phase III Study D8110C00001 To Evaluate Safety And Efficacy Of AZD1222 In Over 30,000 Volunteers



- Given by intra-muscular injection, 0.5 ml
- Study ongoing in the US, Chile and Peru (NCT04516746. ClinicalTrials.gov website)
- Subjects 18+ yo
- 25% subjects 65+ yo

- Study enrollment diversity targets were selected in agreement with US Government/OWS recommendations.

IM = intramuscular; yo = years old.

1- Study NCT04516746. ClinicalTrials.gov website. 2- AstraZeneca Pharmaceuticals LP. Clinical Study Protocol D8110C00001.

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Phase III Study D8110C00001 Diversity And Enrollment

Race	Enrolled[a]
Hispanic/Latin	11.2%
Black or African American	9.8%
Asian	5.3%
American Indian	1.8%
Hawaiian or Pacific Islander	0.4%
White	71.5%

[a]US enrollment only

Age groups and comorbidities[b]	Enrolled
65+ years old	23.6%
<65 years old	76.4%
Has comorbidity	57.8%
No comorbidity	42.2%

[b]Comorbidities include: Chronic Kidney Disease, COPD, Heart Failure, Coronary Artery Disease, Diabetes, Asthma, High Blood Pressure, Liver Disease, BMI 30+.

32,459 participants enrolled; 26,327 received second dose by Jan 21, 2021

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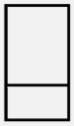
AZD1222 Storage And Administration

Storage



Refrigerator

- Store in refrigerator (2 to 8°C)
- Shelf life = 6 months
- Do not freeze
- Keep vials in outer carton to protect from light

Administration

Multi-dose Vial

- After first puncture cumulatively store up to 6 hours at room temperature or up to 48 hours at 2-8°C with total storage time not to exceed 48 hours.
- No dilution or reconstitution

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Summary: AZD1222 offers a potential to address the Global COVID-19 Crisis

- **AZD1222 induces robust immune responses against the SARS-CoV-2 S protein:**
  - Spike Antibodies increased after a second dose with GMTs comparable to convalescent sera
  - Neutralizing Antibodies titers observed in all participants following 2nd dose
  - Strong Th-1 biased CD4+ T Cell response observed
- **US Phase III study ongoing with 32,459 participants enrolled with co-morbidities, older adults and diverse backgrounds**
  - 26,327 received second dose by Jan 21, 2021
- **Efficacy and safety were demonstrated in four Phase I-III studies in UK, Brazil and South Africa**
- **AZD1222 has the potential to address the SARS-CoV-2 pandemic and has been authorized in 18 countries (under emergency use or full approval as of January 25, 2021)**

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GMT = geometric mean titer.

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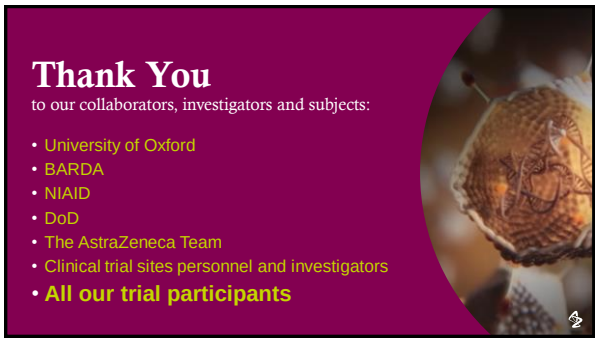

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Phase III Study D8110C00001 Case Definition Of Symptomatic COVID-19 Disease

Primary efficacy endpoint: *Symptomatic illness*

- First case of SARS-CoV-2 RT-PCR-positive symptomatic illness occurring > 14 days post administration of study intervention. Participants included if they meet following criteria at any point from Day 1 (initial visit) through Day 14

Subjects will be counted as a case if they have: 1) One or more category A findings OR 2) Two or more category B symptoms

Specificity (Pathogen Confirmation)	Category A: Lower respiratory tract involvement (one or more)	Category B: Systemic/ other symptoms (two or more)
SARS-CoV-2 confirmed • Positive RT-PCR	• Pneumonia diagnosed by chest x-ray, or CT scan • O_2 sat of ≤ 94% on room air or 2 percentage point drop from baseline • New or worsening dyspnea/ shortness of breath	• Fever > 37.8˚ C (100˚ F) or feverishness • New or worsening cough • Myalgia/ muscle pain • Fatigue that interferes with activities of daily living • Vomiting or diarrhea • Anosmia or ageusia

Safety endpoint:

- Occurrence of adverse events :
  1) Incidence of AEs for 28 days post each dose
  2) Incidence of AEs, MAAEs, and AESIs from Day 1 post treatment throughout study

20 AE = adverse event; AESI = adverse event of special interest; MAAE = medically attended adverse events.
AstraZeneca Pharmaceuticals LP. Clinical Study Protocol D8110C00001.

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Phase III Study D8110C00001 Clinical Hold Summary

- Study was initiated on 28 Aug and paused by AstraZeneca on 6 Sep. Clinical hold was issued on 9 Sep and lifted on 23 Oct; study restarted on 28 Oct
- The study was paused due to an event of transverse myelitis reported in the Phase II/III study conducted by the University of Oxford in the UK
- **Information provided to FDA:**
  - Additional details on neurological events in studies sponsored by AstraZeneca and University of Oxford
  - Analyses of available clinical safety data from AZD1222 and ChAdOx-1 viral vector platform studies
- **Changes in study conduct implemented**
  - Updated risk language in Informed Consent Form (ICF) and Investigator Brochure (IB)
  - Protocol changes
  - Establishment of independent expert neurology panel
  - Accelerated/increased safety reporting

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