Anti-COVID19 VaccinaTion AKS-452X BOOSTER Study (ACT-BOOSTER study)

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Hypothesis: A booster dose of the naked (i.e. non-adjuvanted) 5x concentrated AKS-452X vaccine, will provide an enhanced immune response after vaccination with any of the registered vaccines, either as primary vaccin or booster vaccin, against COVID...

Ethical review	Approved WMO
Status	Completed
Health condition type	Viral infectious disorders
Study type	Interventional

Summary

ID

NL-OMON51511

Source
ToetsingOnline

Brief title
ACT-BOOSTER study

Condition

- Viral infectious disorders

Synonym
COVID-19

Research involving
Human

Sponsors and support

Primary sponsor: Akston Biosciences Corporation
Source(s) of monetary or material Support: Akston Biosciences Corp.;Worcester MA;USA

Intervention

Keyword: AKS-452, Booster, COVID-19, Vaccin

Outcome measures

Primary outcome

Enhanced immune response rate defined as i) at least 80% of all participants demonstrate any increase in IgG titers between Day 0 and Day 28 and ii) the geometric mean ratio of titers from Day 28 to Day 0 should be at least three (3x) times.

Secondary outcome

Safety evaluation for local and systemic adverse events after injection every pre-defined scheduled follow-up (post intervention). Participants will continue to be followed passively for additional safety events out to 9 months post-intervention.

To achieve these objectives, the following will be measured:

o Anti-SARS-CoV-2 SP RBD IgG titers at days 0, 28, 56, 91, 182 and 273 post-boostering.

o Serum titer inhibition of recombinant ACE2-SP/RBD binding and/or neutralization of live SARS-CoV-2 virus infection of live cells (Plaque Reduction Neutralization Test, PRNT) at days 0, 28, and 182

o T-cell responses measured ex vivo using PBMCs to measure SP/RBD-specific T cell production of IFN-* and Th1/Th2/Th17 related cytokines via ELISpot or other Ag-specific flow cytometric-based assays on days 0, 28, and 182.

Study description

Background summary

Every decade in the twenty-first century has experienced a new major coronavirus epidemic; SARS in the 2000s, MERS in the 2010s, and now (2020 and onwards) Coronavirus Disease 2019 (COVID-19) caused by the SARS-COV-2 virus. This novel COVID-19 is a severe and acute respiratory illness caused by infection with the SARS-CoV-2 virus. The first COVID-19 case was reported in Wuhan, China in December 2019 and as of October 5th, 2021, the moment of initiation of this study, there has been approximately 236 million (M) cases world-wide to date (quantified as SARS-Cov-2 virus confirmed and unconfirmed *probable*), in which there are around 4.8 M fatal cases attributed to COVID-19 (COVID-19 Dashboard by the Center for Systems Science and Engineering (CSSE) at Johns Hopkins University; https://www.covidtracker.com/).

Consequently, to address this pandemic crisis, there is an immediate need for solutions that can accurately quantify the level of neutralizing anti-SARS-CoV-2 antibodies (Abs) in individuals and therapeutically induce and/or amplify the level of neutralizing anti-SARS-CoV-2 Abs across the population. The expectation of the foreseeable future is that natural and vaccine-induced immunity most likely will not be long-lived [4, 7-10], and therefore a cost-effective and safe vaccine administered as frequently as every 6 months (boostering), if necessary, is required to maintain robust immunity among the population. Due to the apparent increased transmissibility of SARS-CoV-2, a global security priority is to advance and stockpile coronavirus vaccines as quickly as possible, inevitably requiring significant international funding and relaxing of regulatory paths in a responsible manner. Given the challenges of a recombinant SARS-Cov-2 Spike Protein (SP) subunit vaccine to induce a strong protective immune response in an immunologically naïve human population, the SP Ag must be modified and/or formulated with additional immune-enhancing features to overcome the activation thresholds of naïve T and B cells. Akston has implemented the following features into its COVID-19 vaccine that are major advantages over most other such vaccines in development, in which the Therapeutic Product Profile (TPP) describes details of its clinical candidate, AKS-452:
1. The use of the smaller focused antigenic portion of SP, the RBD
2. Recombinant fusion of RBD with human IgG1 Fc (SP/RBD-Fc)
3. Emulsification of SP/RBD-Fc in the water-in-oil adjuvant, Montanide ISA 720 (only primary vaccine - which is not part of the booster vaccine)
In summary, the Fc moiety on AKS-452 is designed to act as a mild adjuvant via inducing activation signaling to the antigen-presenting cell (APC) via FcypsilonRs to enhance the duration of Ag exposure to APCs and perhaps direct Ag entry into lymph nodes locally and systemically where additional APCs reside. As a consequence, the Fc moiety is expected to create a dramatic dose-sparing potential for both the Ag such that the risk of reactogenicity (a

safety concern) is dramatically reduced; i.e., too much adjuvant that over-activates many APCs and other innate immune cells can lead a systemic inflammatory reaction termed reactogenicity. Such reactogenicity is induced acutely after injection and is not mediated by T and B cells.

Study objective

Hypothesis: A booster dose of the naked (i.e. non-adjuvanted) 5x concentrated AKS-452X vaccine, will provide an enhanced immune response after vaccination with any of the registered vaccines, either as primary vaccin or booster vaccin, against COVID-19

To determine the immunogenicity 4-6 weeks after subcutaneous injection of a booster dose of 90 µg AKS-452X vaccine in people who have previously received any of the registered vaccines against COVID-19 for primary or booster immunization (i.e. Pfizer [Comirnaty], Moderna [Spikevax], Janssen [Ad26.COV2.S], AstraZeneca [Vaxzevria]) in human healthy volunteers.

Secondary objective: Vaccine safety and side effects after booster vaccination.

Study design

Single center, open-label, safety and efficacy study on the biological activity of a SP/RBD-Fc antigen booster vaccine (AKS-452X) against COVID-19.

Intervention

One booster dose-level of naked AKS-452X (90 µg) will be administered via s.c. route to 72 subjects who have only received a primary vaccin, divided in 4 cohorts (one cohort per registered vaccin). Furthermore, a cohort of 150 participants will be included, who have received a primary and booster vaccin. Safety parameters and neutralizing IgG titers will be reviewed after the booster dose of 90 µg s.c.

Main study parameters/endpoints: Enhanced immune response rate defined as i) at least 80% of all participants demonstrate any increase in IgG titers between Day 0 and Day 28 and ii) the geometric mean ratio of titers from Day 28 to Day 0 should be at least three (3x) times.

Secondary endpoints:
Safety evaluation for local and systemic adverse events after injection every pre-defined scheduled follow-up (post intervention). Participants will continue to be followed passively for additional safety events out to 9 months post-intervention.
To achieve these objectives, the following will be measured:

o Anti-SARS-CoV-2 SP RBD IgG titers at days 0, 28, 56, 91, 182 and 273 post-boostering.
o Serum titer inhibition of recombinant ACE2-SP/RBD binding and/or neutralization of live SARS-CoV-2 virus infection of live cells (Plaque Reduction Neutralization Test, PRNT) at days 0, 28, and 182
o T-cell responses measured ex vivo using PBMCs to measure SP/RBD-specific T cell production of IFN-* and Th1/Th2/Th17 related cytokines via ELISpot or other Ag-specific flow cytometric-based assays on days 0, 28, and 182.

Study burden and risks

The burden of participating in the study will be the number of site visits and possible travelling for subjects, study investigations such as blood samples for measurement of immunogenicity, physical examination prior to inclusion / exclusion, and physical discomfort related to the subcutaneous injection of AKS-452X. The majority of AEs associated with exposure to the AKS-452X vaccine, based on the observations of a first in-human phase I/II clinical study using the same AKS-452 vaccine and adjuvant Montanide ISA-720 (ClinicalTrials.gov: NCT04681092) are *injection site reaction,* and *injection site nodule*. All registered AEs are likely to subside within days to weeks after appearance. The future benefit, in the case of a safe and sufficient immunogenicity provoking booster vaccine, is for protecting health care workers, future vulnerable and frail elderly, and patients undergoing large surgical procedures for instance oncology, transplantation etc. Moreover, providing protection in co-morbid citizens (i.e., diabetes, overweight, cardiovascular disease, etc.) and ultimately, creating another leverage to returning societies back to their previous health care system, i.e. low- and middle income countries, capacities and economic growth world-wide.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Age 18-85 years (extremes included), males and females.
- Body mass index (BMI) between 19.0 and 30.0 kg/m2, inclusive
- General good health, without significant medical illness, as determined via physical exam findings, or vital signs
- No clinically significant laboratory abnormalities as determined by the investigator
Note: one retest of lab tests is allowed within the screening window
- Informed Consent Form signed voluntarily before any study-related procedure is performed, indicating that the subject understands the purpose and procedures required for the study and is willing to participate in the study
- Willing to adhere to the prohibitions and restrictions specified in this protocol
- All participants must have received a completed (registered) vaccine or booster at least three months before inclusion in this study (i.e. Pfizer [Comirnaty], Moderna [Spikevax], Janssen [Ad26.COV2.S], AstraZeneca [Vaxzevria]).
- Negative hepatitis panel (including hepatitis B surface Ag and anti-hepatitis C virus Abs) and negative human immunodeficiency virus Ab and Ag screens at screening
- Female subjects should fulfil one of the following criteria:
o At least 1 year post-menopausal (amenorrhea >12 months)
o Surgically sterile (bilateral oophorectomy, hysterectomy, or tubal ligation);
o Will use adequate forms of contraceptives from screening to discharge.
- Female subjects of childbearing potential and male subjects who are sexually active with a female partner of childbearing potential must agree to the use of an effective method of birth control from screening to discharge
o Note: medically acceptable methods of contraception that may be used by the subject and/or partner include combined oral contraceptive, contraceptive

vaginal ring, contraceptive injection, intrauterine device, etonogestrel implant, double barrier, sterilization and vasectomy
- Female subject has a negative pregnancy test at screening and upon check-in at the clinical site.
o Note: pregnancy testing will consist of a serum pregnancy test at screening and urine pregnancy tests at the dosing visit, in all women.

Exclusion criteria

- Pregnant or breast-feeding females
- Evidence of clinically significant neurologic, cardiac, pulmonary, hepatic, hematologic, rheumatologic, endocrine, autoimmune, or renal disease
- Any laboratory test which is abnormal, and which is deemed by the Investigator(s) to be clinically significant
- Behavioral or cognitive impairment or psychiatric disease that in the opinion of the investigator affects the ability of the subject to understand and cooperate with the study protocol
- Current alcohol/illicit drug/nicotine abuse or addiction: history or evidence of current drug use or addiction (positive drug screen for amphetamines, barbiturates, benzodiazepines, cannabinoids, cocaine, or opiates) or signs of excessive use of alcohol at screening and at day 0.
- Presence of any febrile illness (T > = 38.0°C or lab confirmed viral disease (PCR)) or symptoms suggestive of a viral respiratory infection within 1 weeks prior to vaccination. Participants will be screened for SARS-Cov-2 with an EUA-approved PCR test at screening, and at day 0.
- Use of corticosteroids (excluding topical preparations for cutaneous or nasal use) or use of immunosuppressive drugs within 30 days before inoculation
- A history of anaphylaxis, history of allergic reaction to vaccine, known allergy to one of the components in AKS-452X. Mild allergies without angio-edema or treatment need can be included if deemed not to be of clinical significance (including but not limited to allergy to animals or mild seasonal hay fever)
- A history of asthma within the past 10 years, or a current diagnosis of asthma or reactive airway disease associated with exercise
- Receipt of blood or blood-derived products (including immunoglobulin) within 6 months prior to vaccination.
- Receipt of another investigational agent within 30 days or 5 times the product half-life (whichever is longest) prior to vaccination
- Deprived of freedom by an administrative or court order or in an emergency setting
- Any condition that in the opinion of the principal investigator (PI) would jeopardize the safety or rights of a person participating in the trial or would render the person unable to comply with the protocol.

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	12-05-2022
Enrollment:	222
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	AKS-452X

Ethics review

Approved WMO Date:	01-02-2022
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	10-02-2022
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	03-03-2023

Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2021-005509-28-NL
CCMO	NL79397.000.21

Study results

Date completed:	15-03-2023
Results posted:	13-09-2024
Actual enrolment:	71

First publication
01-01-1900