Supplementary Appendix

Contents

Study inclusion and exclusion criteria

Inclusion criteria

- Healthy as determined by the investigator or medically-qualified designee based on a medical evaluation including medical history, physical examination, and laboratory tests.
- Men and women aged 18–65 years.
- A female subject was eligible to participate if she was not pregnant (as confirmed by a negative serum or urine human chorionic gonadotropin test), not lactating, and at least one of the following conditions applied:
    - Non-reproductive potential, defined as: 1) premenopausal females with one of the following: documented tubal ligation; documented hysteroscopic tubal occlusion procedure with follow-up confirmation of bilateral tubal occlusion; hysterectomy; and documented bilateral oophorectomy; 2) postmenopausal defined as 12 months of spontaneous amenorrhoea. Females on hormone replacement therapy (HRT) and whose menopausal status was in doubt were required to use a highly-effective contraceptive method if they wished to continue their HRT during the study. Otherwise, they had to discontinue HRT to allow confirmation of postmenopausal status prior to study enrolment.
    - Reproductive potential and agreement to follow a highly-effective contraceptive method from 30 days prior to the first dose of study medication until after the last dose of study medication and completion of the follow-up visit at Day 183 (at least 5 terminal half-lives for raxibacumab).

Exclusion criteria

A subject was not eligible for inclusion if any of the following criteria applied:

- Previously vaccinated against PA.
- Anti-PA Ab concentration >2 times the lower limit of quantitation (LLoQ) at screening.
- Concurrent participation in another clinical study at any time during the study period, in which the subject had been or would have been exposed to an investigational or non-investigational study vaccine/product (pharmaceutical product or device).
- A member of the military, a laboratory worker, first responder, health care worker, or those who would otherwise be at higher risk of exposure to anthrax.
- History of regular alcohol consumption within 1 month of the study.
- Alanine transaminase and bilirubin >1·5 x upper limit of normal (ULN) (isolated bilirubin >1·5 x ULN was acceptable if bilirubin was fractionated and direct bilirubin was <35%).
- Current or chronic history of liver disease or known hepatic or biliary abnormalities (with the exception of Gilbert's syndrome or asymptomatic gallstones).
- Any confirmed or suspected immunosuppressive or immunodeficient condition resulting from disease (e.g. malignancy, human immunodeficiency virus (HIV) infection) or immunosuppressive/cytotoxic therapy (e.g. medications used during cancer chemotherapy, organ transplantation or to treat autoimmune disorders).
- Presence of hepatitis B surface antigen, positive hepatitis C Ab test results at screening or within 3 months prior to first dose of study treatment.
- Positive pre-study drug/alcohol screen.
- Positive test for HIV Ab.
- History of sensitivity to any of the study medications, or components thereof (especially latex and aluminum) or a history of other known drug allergies that, in the opinion of the investigator or GSK Medical Monitor, would have contraindicated their participation.
- Administration of Ig not included in this trial and/or any blood products within 3 months preceding the first dose of study vaccine or planned administration during the study period.
- Administration of long-acting immune-modifying drugs (e.g. infliximab) within 6 months prior to the first vaccine dose or expected administration during the study period.
- Chronic administration (defined as >14 consecutive days) of systemic immunosuppressants or other immune-modifying drugs within 6 months prior to the first vaccine dose. Inhaled, topical, and intra-articular corticosteroids were allowed.
- Administration or planned administration of a vaccine not foreseen by the study protocol within the period starting 35 days prior to the first dose of study vaccine(s) and ending 30 days after the last dose of study vaccine. This included any type of vaccine such as (but not limited to) live, inactivated and subunit vaccines. Influenza vaccines were permitted after Week 8.

- Willing to abstain from taking pre-specified prescription or non-prescription drugs.
- Exposure to >4 new chemical entities within 12 months prior to the first dosing day.
- Any condition which, in the opinion of the investigator, would have prevented the subject from participating in the study.

Assays

Anti-PA assay

The reference standard was supplied by the US Centers for Disease Control and Prevention (CDC) (BPR-6004-00, Lot# 1001 MPIR-3004) and used to construct the calibration curve over the range 5 to 100 µg/mL in Tris assay buffer (surrogate matrix). The method involved dilution of serum samples at a minimum required dilution of 1:2500 followed by the immunodepletion of raxibacumab using a biotinylated mouse anti-raxibacumab mAb (mouse hybridoma; Clone 1D4.5G6) on the Kingfisher Flex automated system (ThermoScientific). Briefly, the biotinylated mAb was bound to magnetic streptavidin coated beads (Dynabeads MyOne Streptavidin [Invitrogen]), washed four times in Tris assay buffer (25 mM Tris, 150 mM NaCl, 0·1% BSA, 0·1% Tween 20, pH 7·5) and incubated with the diluted serum samples for approximately 1 hour at 37°C. The raxibacumab depleted samples, containing endogenously derived anti-PA antibodies (Abs), were quantitated by electrochemiluminescent (ECL) immunoassay after capture from the depleted serum sample using recombinant PA from *B. anthracis* (List Biological Laboratories cat#171B) and detected by anti-human IgG Ab (MSD™ Sulfo Tag Anti-Human (goat) 0·5 mg/mL; MSD™ Cat#R32AJ-1).

The assay had a validated range of 5·0 to 100 µg/mL for endogenous Abs to anthrax PA in human serum. At all validation sample concentrations, the accuracy, expressed as percentage bias, was less than the a priori defined acceptable level of 20% (25% at the LLoQ). The maximum percent bias observed for surrogate matrix was -10·9%. The maximum percent bias observed for human serum was -5·2%. The within run precision values were <20% (25% at the LLoQ). The maximum observed within-run and between-run precision for surrogate matrix was 8·6 % and 4·9, respectively, while the maximum observed within-run and between-run precision for human serum was 6·6 % and 2·3 %, respectively. For study support, quality control samples were prepared using CDC reference standard in surrogate matrix, blank human serum (authentic matrix) and pooled serum samples derived from the study.

Toxin neutralising activity assay

This assay to measure toxin neutralising Abs has been described previously[1] and is based on a published procedure.[2] The in vitro assay is based on the principle that PA neutralising Abs can protect living cells (mouse macrophage, J744A.1) that have been exposed to anthrax toxin. Each test sample is represented by a titre value, defined as sample effective dose ED50, which correlates with the ability of the sample to protect cells by neutralising PA, thus preventing the formation of lethal toxin.

Briefly, J774A.1 cells (ATCC Lot#60378631) were grown in culture from a frozen vial of cells banked at passage 3 (from original stock) and passed at least 3 times in growth media prior to use in the assay. The cells were added to a tissue culture treated plate at $2{\cdot}25x10^5$ cells/mL (100 µL/well) and incubated overnight (16–24 hours) at 37±5°C with 5±2% CO_2. On the same day, samples and controls were serially diluted with assay media, further diluted 1:25 in assay media and incubated at 2–8°C overnight. The next day samples were incubated with a solution of PA (PA – HGS, Lot# LD-100666) and Lethal Factor (LF – HGS, Lot#LD-100703) for 45±15 minutes and then placed onto the live cells for 4 hours±15 minutes. Afterwards, MTT dye was added to the cell plate, followed by a stop solution 2 hours±10 minutes later. Plates were left to stabilise overnight before being read on a Spectramax plate reader at wavelengths of 570 and 690 Lm. The negative control (NC) was a normal human serum pool created from serum samples from drug-naïve healthy human donors. The positive control (PC) was raxibacumab 62·5µg/mL in normal human serum pool.

SoftMax PRO (version 5·0 or higher) is used to calculate the mean optical density (OD), standard deviation (SD) and % coefficient of variance (%CV) for all control and sample replicates. The data calculations are performed in SoftMax PRO (version 5·0 or higher) to determine the ED50 (titre) of the individual samples on the 4-PL curve by fixing the upper asymptote with sample mean value (without lethal toxin) or NC mean value (without lethal toxin) for sample and PC, respectively. The lower asymptote for samples and PC is set as the last dilution's mean value of the corresponding sample or NC, respectively. The PA neutralising Abs prevent the formation of lethal toxin. If no neutralising Abs are present, lethal toxin complexes enter the cells and cause cell death. Increased cell

viability correlates with inhibition of PA binding and is used to determine the relative titre of serum samples compared with a known positive control (62·5µg/mL raxibacumab).

For assessing assay precision and specificity, two analysts performed a total of three runs and each run was three plates. The validation limit for both intra-assay and inter-assay precision was pre-defined as ≤30% CV; the intra-assay precision for positive control samples ranged from 10·0 to 22·4% CV. For inter-assay precision of positive control samples, the CV was 29·5%. The assay is accurate up to the 1:4 dilution of the positive control. Subsequently, this dilution was used to determine the minimum OD acceptable for calculating a titre, and the titre that defines the assay LLoQ. The minimum OD needed for an accurate titre calculation is 0·595. Any sample where the average OD of the first dilution is below this will not be assigned a titre value and will be considered below LLoQ. The titre that defines LLoQ is 25·9.

Raxibacumab PK assay

The method for determination of raxibacumab utilised immunocapture purification using proprietary mouse anti-raxibacumab Ab (Hybridoma-Clone # ID4·5G6). The capture reagent (mouse anti-raxibacumab Ab) was biotinylated with EZ-link™ Sulfo-NHS-LC-Biotin (Thermo Scientific, cat. # 21327) in excess of biotin and desalted by rinsing through the Zeba spin column (Thermo Scientific, cat. # 89890) with 1XPBS (Gibco, cat. # 10010-023). Next, the capture reagent was incubated in a streptavidin microtitre plate (Pierce, cat. # 15502) with constant shaking for approximately 1 hour at 37°C. After the wash step, standards, quality controls, and samples (100 µL) were added to the streptavidin microtitre plate and incubated with constant shaking for approximately 2 hours at 37°C. Following the completion of biotinylated mouse anti-raxibacumab Ab incubation with samples, the plates were washed and underwent a reduction step, by adding 50 µL DTT (Sigma, cat. # 646563; shaking for 1 h at 60°C), and an alkylation step, by adding 10 µL 2-chloroacetamide alkylating reagent (Sigma, cat. # 22790-250G-F; shaking for 30 min at ambient temperature). Next, 100 µL of trypsin digestion buffer (Thermo Scientific, cat. # 90059) was added to each well of the streptavidin microtitre plate containing a double-blank sample. In addition, 100 µL of trypsin digestion buffer containing an internal standard (IWGR[F_13C915N]EYWGRGTTV; Sigma, AQUA peptide custom order) was added to each well of the streptavidin microtitre plate containing the blank with internal standard, calibration standards, quality controls/validation samples or unknown samples. Plates were incubated with constant shaking for 18–24 hours at 37°C. Following the digestion, 90 µL of the sample was transferred into a tube containing 10 µL of 10% formic acid. After the mixing and brief centrifugation step, samples were injected onto liquid chromatography–mass spectrometry for quantitation of the representative peptide 'FEYWGR' by UHPLC-MS/MS using a TurboIonSpray™ interface and multiple reaction monitoring.

At all validation sample concentrations examined, the bias was less than the pre-defined acceptable level of 20% (25% at the LLoQ); the maximum bias observed was 7·4%. At all validation sample concentrations examined, the within- and between-run precision values were ≤20% (25% at the LLoQ); the maximum within- and between-run precision values observed were 16·7% and 3·1%, respectively. As defined by the lower and upper validation sample concentrations possessing acceptable accuracy and precision, the validated range of this method is 250 to 50000 ng/mL based on 10 µL of human serum.

Raxibacumab immunogenicity assay

The assay included a 3-step process for determination of anti-raxibacumab Abs in human serum samples. The first analysis consisted of a screening test to identify potential positive samples. If a test sample was identified as a potential positive, the specificity of the response was evaluated in a confirmation assay. Any sample that was confirmed as positive was further analysed in a titration assay to quantify the level of anti-raxibacumab Abs in the sample.

Measurement of anti-raxibacumab Abs was conducted using a bridging ECL immunoassay in which biotinylated raxibacumab, ruthenylated raxibacumab, and serum samples were pre-incubated overnight and added to a pre-blocked streptavidin MSD plate. The plate was incubated for 1 hour and after addition of MSD read buffer, the ECL signals were measured.

Statistical analysis and description of the interim analyses

Sample size assumptions

The sample size calculation is based on the assumption that the individual values will be analysed after being transformed by $\log_{10}$ resulting in data that is approximately normal. In the transformed data the analysis of the ratio of the means is equivalent to a difference of mean values with a margin of $\log_{10}$ (1·5) = 0·176. The SD of the $\log_{10}$ transformed data is assumed to be 0·75. This is selected based on the fact that the sample size in the study by Marano [3] was based on a SD of 0·45 based on the data from the study by Pittman[4], but the results from the Marano study had higher SDs suggesting an estimate closer to 0·85.[3]

The sample size is calculated assuming 1:1 randomisation and two interim analyses for futility after 30 and 100 analysable subjects. The boundaries for the futility analysis are based on Rho family error spending function with a Rho of 0·5. For the purposes of the sample size calculation, the power was calculated under the alternative hypothesis setting, where the ratio is 1, or equivalence between the two arms with respect to concentrations of anti-PA Ab. With a type 1 error of 5% one-sided a sample size of 534 subjects allowed for 80% power to make a claim of non-inferiority (margin of 1·5), if the true ratio between the geometric means is 1. In a trial of 534 patients, the largest observed GMC ratio between the AVA and the combination that results in a statistically significant non-inferiority result is an estimated ratio of 1·173. This can alternatively be viewed as a minimum observed anti-PA concentration due to the addition of AVA in the combination of ~85% of the concentration when AVA is administered alone. This is under the assumption that the observed variability in the study population is similar to the study design assumption.

Interim analyses

Two interim analyses were planned to allow early study termination if a large effect of raxibacumab on AVA immunogenicity was confirmed at the interim. The first interim analysis was performed after 30 evaluable subjects and the second interim was performed after the first 100 evaluable subjects had reached the Week 4 endpoint. These interim analyses were performed on the PP population by independent statistical and medical personnel using unblinded data. For the interim analyses, immunogenicity data were summarised by ratio of GMC of anti-PA Ab concentrations with corresponding 95% CI. A two-sample *t*-test for the log transformed data was performed and a corresponding p-value was provided, which was used to determine if the futility threshold had been crossed at the respective interim analyses. The study would have been terminated early if the futility boundary was crossed at an interim; otherwise, recruitment was to continue for the next phase.

Final analyses

Anti-PA Abs

At the final analysis, the non-inferiority test was based on the CI for the ratio of anti-PA Ab (attributable to AVA) GMCs between the AVA and the AVA plus raxibacumab groups at Week 4. This analysis was performed in the PP population. If the upper bound of the 90% CI was <1·5, non-inferiority would have been established.

GMCs of the anti-PA Abs for each treatment group were summarised with corresponding 95% CI for Weeks 4, 8, and 26. Ratios of the anti-PA Abs GMC for each treatment group at Weeks 4, 8, and 26 were also tabulated. This analysis was repeated in two sensitivity analyses which used the ITT population with imputation for subjects without Week 4 anti-PA Ab concentration results. Welch's unequal variances *t*-test was performed to assess the sensitivity of the results to the assumption of equality of variances between the anti-PA Ab concentrations in the two treatment groups. Values below the LLoQ (5 μg/mL) were set to the LLoQ for calculation of summary statistics.

Toxin neutralising activity

Toxin neutralising activity (TNA) geometric mean titre and 95% CI were summarised for each treatment group at each time point. The percentage of subjects who seroconverted (≥4-fold increase in TNA titre from baseline) was summarised at Weeks 4, 8, and 26. Values below the LLoQ (25·2) were set to the LLoQ for calculation of summary statistics.

Non-compartmental analysis of PK data

The PK population comprised all evaluable subjects who received raxibacumab and who had at least one post-dose concentration assessment at a scheduled PK time point without events or protocol deviations with the potential to affect PK concentrations. Individual raxibacumab concentration versus time profiles were summarised in a graphical and tabular format based on nominal collection time. Non-compartmental analysis was performed using standard procedures in Phoenix® WinNonlin® Version 6·4 (Certara, L.P. Princeton, NJ, US). Relevant PK

parameters, including the area under the concentration versus time curve ($AUC_{0-\infty}$), maximum concentration (C_{max}), elimination half-life ($t_{1/2,z}$), mean residence time (MRT), clearance (CL), and volume of distribution at steady state (V_{SS}) were derived for each subject and summarised by descriptive statistics. The C_{max} and the time to its first occurrence (T_{max}) were obtained directly from the concentration-time data. The apparent terminal phase rate-constant was used to obtain the $t_{1/2,z}$ and was derived by linear regression of logarithmically transformed concentration versus time data. The area under the concentration-time curve from zero time (pre-dose) to the time of last quantifiable concentration (AUC_{0-t}) and extrapolated to infinity ($AUC_{0-\infty}$) were calculated by logarithmic trapezoidal methods. Five subjects who had no post-dose concentration at a scheduled PK time point, 1 subject who received the incorrect dose due to an AE during infusion, and 1 subject who was administered an incorrect dose were excluded from the PK population. Values below the LLoQ (0·250 μg/mL) were set to LLoQ for calculation of geometric mean, geometric SD, geometric CV%, geometric mean – SD and geometric mean + SD.

PK simulations

To compare the observed PK profiles in this study with those obtained previously in healthy subjects receiving an IV dose of 40 m/kg raxibacumab, 500 simulations were performed using population PK parameter estimates to generate the predicted median concentration versus time profile along with the 95% CIs. Simulations were implemented in NONMEM version 7·3 (ICON Development Solutions Ltd, MD, USA). Raxibacumab population PK was described by a two-compartment model with zero-order infusion and first-order elimination. Body weight as a covariate on clearance, peripheral and central volume of distribution, and intercompartmental clearance.[5]

Safety analysis

Clinical safety observations including AEs, SAEs, urinalysis, vital sign measurements, and clinical laboratory evaluations were tabulated.

Table S1. Concomitant medications reported in >5 subjects in either treatment group (ITT population).

Demographics	**Number (%) of subjects**	
	AVA (N=287)	**AVA plus raxibacumab (N=286)**
Any medication	**133 (46·3)**	**283 (99·0)**
Diphenhydramine as premedication	1 (0·3)	283 (99·0)
Ethinylestradiol	36 (12·5)	32 (11·2)
Paracetamol	25 (8·7)	11 (3·8)
Ibuprofen	20 (7·0)	21 (7·3)
Levonorgestrel	4 (1·4)	12 (4·2)
Vitamins supplements	7 (2·4)	9 (3·1)
Acetylsalicylic acid	7 (2·4)	4 (1·4)
Sodium chloride	3 (1·0)	8 (2·8)
Naproxen	7 (2·4)	2 (0·7)
Sulfamethoxazole	6 (2·1)	6 (2·1)
Benadryl (diphenhydramine) as concomitant medication	4 (1·47)	6 (2·1)
Etonogestrel	5 (1·7)	6 (2·1)
Medroxyprogesterone acetate	5 (1·7)	5 (1·7)
Prednisone	5 (1·7)	0

AVA, anthrax vaccine adsorbed; ITT, intent-to-treat.
Some subjects who took diphenhydramine in addition to the dose administered as study pre-medication were collated under the Preferred Term Benadryl (which is one of the brand names for diphenhydramine). Due to this discrepancy, these subjects have been added to the concomitant list as having been administered Benadryl, rather than diphenhydramine.

Table S2. Sensitivity analysis of GMCs for anti-PA Ab (µg/mL) using the ITT population.

Sensitivity analysis	AVA (N=287) Geometric mean (95% CI)	AVA plus raxibacumab (N=286) Geometric mean (95% CI)	Ratio of geometric means	90% CI	p-value[1]
Week 4 (ITT population)					
Imputation Method 1[2]	26·9 (24·0, 30·2)	22·5 (20·2, 25·0)	1·20	(1·05, 1·37)	0·0026
Imputation Method 2[3]	27·6 (24·5, 31·2)	21·9 (19·6, 24·5)	1·26	(1·10, 1·44)	0·0177

AVA, anthrax vaccine adsorbed; CI, confidence interval; GMC, geometric mean concentration; ITT, intent-to-treat.

[1]p-value results based on a one-sided, two-sample *t*-test for the null hypothesis that AVA/AVA plus raxibacumab ≥1·5 versus that AVA/AVA plus raxibacumab <1·5.

[2]In the AVA arm, missing data are imputed with the third quartile from the non-missing data in this arm. In the AVA plus raxibacumab arm, missing data are imputed with the first quartile from the non-missing data in this arm.

[3]In the AVA arm, missing data are imputed with the maximum from the non-missing data in this arm. In the AVA plus raxibacumab arm, missing data are imputed with the maximum from the lower limit of quantitation.

Table S3. Summary of all serious treatment-emergent AEs in either treatment group (safety population).

	Subjects, n (%)	
	AVA group (n=286)	**AVA plus raxibacumab group (n=280)**
Any serious treatment-emergent AE	5 (1·7)	3 (1·1)
Abortion spontaneous	2 (0·7)	0 (0)
Bile duct stone	0 (0)	1 (0·4)
Cholecystitis	0 (0)	1 (0·4)
Cholelithiasis	0 (0)	1 (0·4)
Bronchitis	0 (0)	1 (0·4)
Completed suicide[1]	0 (0)	1 (0·4)
Asphyxia[1]	0 (0)	1 (0·4)
Respiratory failure	0 (0)	1 (0·4)
Toxicity to various agents[2]	1 (0·3)	0 (0)
Rhabdomyolysis	1 (0·3)	0 (0)
Suicidal ideation	1 (0·3)	0 (0)

AE, adverse event; AVA, anthrax vaccine adsorbed; SAE, serious adverse event.
[1]Subject committed suicide by hanging; the SAE term 'suicide (injury asphyxiation)' was entered as two separate SAEs ('completed suicide' and 'asphyxiation') with the same onset, resolution and outcome of events.
[2]Subject was found dead at home due to drug intoxication (combined fentanyl and methamphetamine intoxication).
A subject may have had >1 AE; a subject experiencing multiple occurrences of an AE was counted, at most, once per Preferred Term. Percentages are based on number of subjects in the Safety population.

Table S4. Summary of selected serum raxibacumab PK parameters in the AVA + raxibacumab treatment group (PK analysis population, N=279)

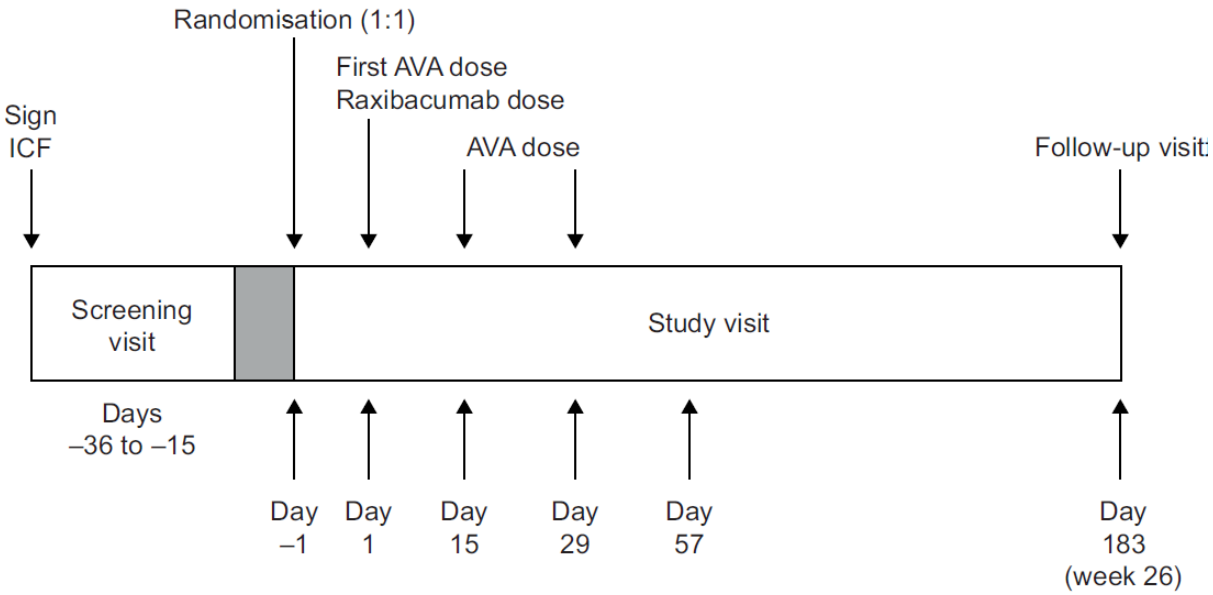
PK parameter	n	Mean ± SD	Median (Range)	Geometric mean [CV%]
$AUC_{(0\text{-}inf)}$ (μg*day/mL)	271	20418·9 ± 4367·7	20335·6 (11376, 42255)	19972·7 [21·3]
$AUC_{(0\text{-}t)}$ (μg*day/mL)	264	20327·4 ± 4326·1	20294·3 (11106, 40320)	19881·2 [21·4]
C_{max} (μg/mL)	277	1184·5696 ± 226·6294	1180·8340 (676·670, 1869·790)	1162·7148 [19·7]
t_{max} (h)	273	4·728 ± ND	2·850 (2·67, 359·17)	ND [ND]
t_{last} (h)	278	4114·530 ± ND	4368·120 (670·72, 4560·12)	ND [ND]
Lambda_z (1/h)	272	0·0012699 ± 0·0003003	0·0012313 (0·000674, 0·002932)	0·0012395 [21·8]
$t_{1/2}$,z (day)	272	23·826 ± 4·956	23·456 (9·85, 42·86)	23·300 [21·8]
MRT (day)	271	28·01 ± 6·73	27·41 (12·2, 57·3)	27·23 [24·3]
CL (mL/day)	271	167·41 ± 46·64	160·27 (81·8, 404·7)	161·47 [27·3]
V_z (mL)	271	5587·8 ± 1297·6	5579·7 (2770, 9814)	5439·5 [23·7]
V_{ss} (mL)	271	4513·9 ± 1034·5	4437·3 (1726, 8888)	4397·0 [23·5]

AVA, anthrax vaccine adsorbed; CL, clearance; C_{max}, maximum concentration; CV%, coefficient of variation; $t_{1/2,z}$, elimination half-life; MRT, mean residence time; ND, not determined; PK, pharmacokinetics; SD, standard deviation; T_{max}, time to maximum clearance; V_{ss}, volume of distribution at steady state; V_z, apparent volume of distribution during terminal phase.

Anti-raxibacumab Abs

There were 37 (12·9%) subjects with low-level detectable anti-raxibacumab Ab values (range: 0·005–<5). Because anti-raxibacumab Abs in these subjects was not consistently detected across different sampling timepoints, these findings were not thought to be clinically significant.

Figure S1. Study design



AVA, anthrax vaccine adsorbed; ICF, informed consent form.

Subjects were randomised to receive either AVA or AVA plus raxibacumab and began the study with a screening visit at 2 weeks to 35 days before the start of study treatment on Day 1 (Days -36 to -15). Results of the screening test for the anti-PA Ab levels were made available prior to randomisation on Day 1. Beginning with the screening visit, the total duration of study for each subject was approximately 28 to 31 weeks. The study duration was selected because it allowed for assessment of the durable immune response to AVA.

Supplementary references

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