Protocol and Statistical Analysis Plan for the Ketamine for AnaLgesia in MEchanically Ventilated Adults (KALME) trial

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Introduction

In Australia and New Zealand, mechanically ventilated patients account for approximately 35% of all adult patients admitted to the intensive care unit (ICU).[1] Pain and discomfort are reported in up to 71% of such patients.[2, 3] International clinical practice guidelines recommend the use of opioids to manage pain and to aid with sedation in such patients, so called analgosedation.[4]

However, opioid use in patients receiving mechanical ventilation has been associated with in hospital delirium in over 40% of patients, and with long-term opioid use.[5, 6] Adjuncts to analgosedation may reduce the exposure to opioids and decrease such risks. Ketamine has favourable properties which make it an attractive adjunct to opioid analgosedation.

Ketamine was first synthesised almost 60 years ago and is similar in structure to the psychotropic agent phencyclidine.[7, 8] Ketamine is a selective, non-competitive, NMDA receptor antagonist, with analgesic properties at lower dose and dissociative anaesthetic properties at higher dose.[9-11] Ketamine has been recommended for use as an opioid sparing agent to treat pain and discomfort in mechanically ventilated surgical ICU patients. However, such a recommendation is only “conditional”, because of very low quality of evidence.[4]

Accordingly, we designed a prospective, randomised, double-blind, placebo-controlled pilot trial of ketamine for adjunct analgosedation in mechanically ventilated ICU adults. Our aim is to assess the effect of adding ketamine for analgosedation on the use of opioid medications in mechanically ventilated patients. Our hypothesis is that ketamine will decrease the use of fentanyl equivalents. We are also testing the feasibility of conducting a clinical trial of ketamine and to inform further work in this area.

Methods

Study design and setting

The KALME trial is a multicentre, prospective, double-blind, placebo controlled randomised pilot trial with 1:1 allocation assessing the effect of an intravenous (IV) infusion of ketamine on opioid requirements in mechanically ventilated ICU patients. The study is being conducted at two university-affiliated ICUs in two hospitals in Melbourne, Australia (Austin Hospital in Heidelberg and The Northern Hospital in Epping). Recruitment began in September, 2022 and as of the 6th May, 2024, 103 patients have been enrolled into the trial. It is expected that recruitment will cease in July, 2024.

Ethics

The protocol was approved by the Human Research Ethics Committee (HREC/83652/Austin-2022) and the trial registered with the Australian New Zealand Clinical Trials Registry (ACTRN12622000920796). A process of delayed consent was applied.

Inclusion Criteria

1. Age ≥ 18 years;
2. Mechanically ventilated;
3. Opioid medication infusion prescribed by treating ICU physician; and
4. Enrolment within 12 hours of ICU admission.

Exclusion Criteria

1. Cardiac Surgical patients;

2. Previous adverse reaction to ketamine;
3. Age ≥ 80;
4. Pregnancy or lactation;
5. Uncontrolled hypertension (SBP > 180 mmHg);
6. Uncontrolled heart failure or cardiogenic shock;
7. Patients admitted for end-of-life care or to facilitate organ donation;
8. Previous enrolment in the KALME trial; or
9. No legal surrogate identified or able to provide informed consent to continue for patient.

Randomisation

Patients are screened for eligibility on admission to ICU and/or commencement of mechanical ventilation and opioid infusion. Patients excluded from the study have the reason documented in a standard CRF.

The randomisation list was computer generated, using permuted blocks, and stratified by hospital, age (< 65 or ≥ 65 years) and sex (female or male). Randomisation occurs via a password-protected encrypted web-based interface (Redcap), and patients are required to be randomised within 12 hours of ICU admission.

Treatment masking (blinding)

Patients, medical treatment decision makers, medical, allied health and nursing staff caring for the patients, data collectors, and the trial statistician are all blinded to trial group assignment. Unblinding of a patient's allocated study treatment is only performed when knowledge of the treatment allocation influences the participant's

management in a significant fashion. The treating clinician or investigator contacts the coordinating body if they consider a need for unblinding, and this may be adjudicated by the study management committee.

Intervention

Patients are allocated to receive intravenous ketamine via continuous infusion vs. placebo. Ketamine infusions are prepared by ICU nursing staff in a solution of 200 mg of ketamine in 100 mL of 0.9% NaCl (final concentration, 2 mg/ml). For the purposes of the study, the formulations are prepared by staff not directly involved in the patient care. The trial drug and placebo have identical packaging with attached label: “KALME Trial Drug Number XXXX”.

Patients receive approximately 0.15 mg/kg/hr (0.075 ml/kg/hr) actual body weight (to a maximum equivalence of 100 kg or 15 mg/hr) of trial drug infusion without bolus due to concerns regarding side effects (**Table 1**). Patients receive the trial drug while they are receiving opioid infusions during mechanical ventilation. Cessation of the trial drug occurs when:

1. Opioid infusion is ceased;
2. Patient is extubated and mechanical ventilation ceased;
3. Patient has goals of care changed to end-of-life/comfort care;
4. In the event of adverse effects believed to be due to the trial medication;
5. Death or discharge from ICU.

Treating medical staff can continue the trial medication after opioid cessation whilst ventilated or for a period of up to 12 hours post extubation. Open label ketamine infusion can be administered following extubation if indicated by the treating team for

analgesic effect. The trial drug is administered during the first episode of mechanical ventilation and only during the first ICU admission.

Apart from the inclusion of the trial medication, day to day management including use and dose of all other medications including sedatives, analgesics and anti-psychotic medications is at the discretion of the treating teams. In addition, ventilatory management, weaning and extubation plan is determined by the treating physicians. As per local protocols, all patients have four hourly Richmond Agitation Sedation Scale (RASS), eight hourly Critical Care Observation Tool (CPOT) and daily CAM ICU scores assessed.

Primary outcome

The primary outcome is the hourly dose of opioids used as an infusion during mechanical ventilation, determined by fentanyl equivalents and reported as μg/h. The two drugs commonly used are fentanyl and morphine and they will be compared based on previous data at a ratio of fentanyl:morphine at 10 μg: 590 μg.[12]

Secondary outcomes

The following secondary outcomes will be assessed:

1. Feasibility outcomes (enrolment rate, protocol compliance, and protocol violations);
2. Ventilator free days to day 28 (defined as 28 minus duration of ventilation with non-survivors receiving 0 ventilator free days);
3. Duration of ventilation in survivors (in days);
4. ICU-free days at 28 days (defined as 28 minus ICU length of stay in days with non-survivors receiving 0 ICU-free days);

5. Hospital-free days at 28 days (defined as 28 minus hospital length of stay in days with non-survivors receiving 0 Hospital-free days);
6. Incidence of hallucination (identified using natural language processing);
7. Tracheostomy use;
8. Incidence of delirium (diagnosed using CAM-ICU);
9. ICU length of stay;
10. Hospital length of stay;
11. ICU mortality;
12. Hospital mortality;
13. 28-day hospital mortality;
14. Discharge use of opioid medication; and
15. Use of opioid medication 3 and 6 months after hospital discharge.

Process of care measures

The following process of care measures will be assessed:

1. Dosage of other sedative agents (including propofol, midazolam and dexmedetomidine) during mechanical ventilation;
2. Use of other adjunct medications for analgesia (including paracetamol and NSAIDS);
3. Pain scores;
4. Sedation level (assessed using RASS); and
5. Use and dosage of antipsychotic medications (quetiapine, haloperidol, and olanzapine) during hospital stay.

Adverse events

Any adverse event requiring cessation of the trial drug (including: tachyarrhythmia, hypertension [systolic blood pressure > 180], agitation or severe delirium) will be documented and reported.

Data management

The following data will be collected from data submitted to the Australian and New Zealand Intensive Care Society Centre for Outcome and Research Evaluation (ANZICS CORE):

- Age;
- Gender;
- Body weight and height;
- Admission type (medical vs. elective surgery vs. emergency surgery);
- ICU admission source;
- Chronic co-morbidities;
- APACHE-III admission diagnosis;
- APACHE II and III scores;
- Vital signs and lab results in the first 24 hours;
- Number of mechanical ventilation episodes during the admission;
- Use of vasopressor therapy;
- Use of renal replacement therapy.

Patients who were using either regular or intermittent opioid medications prior to hospital admission will be identified based on hospital admission documentation. Censoring of all hospital related study end points will apply at the time of hospital discharge following the index ICU admission. Long term use of narcotics will be censored at 6 months post hospital discharge.

Information about long term opioid use will be obtained from SafeScript, a Victorian government computer software, in compliance with obligations under the Privacy and Data Protection Act 2014 (Vic) and the Health Records Act 2001 (Vic).

Sample size calculation

A sample size of 120 patients (60 per group) will have 80% statistical power to show a difference of 35% in the mean hourly dose of opioid from an estimated baseline mean hourly dose of 67.0 ± 39.0 μg/h (to an expected mean hourly dose of 43.6 μg/h), considering an alpha of 0.05 and allowing for a 10% dropout.

Analysis plan

The KALME trial was designed and commenced recruitment as a classical frequentist trial. Bayesian methods allow estimation of the probability of different magnitudes of treatment effect, which clinical researchers may interpret more easily than statements from conventional frequentist statistical models about rejection or not of a null hypothesis. Without knowledge of any accumulated trial outcome data, and at ~75% of the initial target sample size (as of 01 May 2024), the KALME trial management committee has initiated a change for the KALME primary and secondary outcomes from the former frequentist models to corresponding Bayesian models. Importantly, there are no changes to any other components of the KALME trial design's inclusion and exclusion criteria, randomization, blinding, treatment, sample size and follow-up. These modifications to KALME will not result in a Bayesian re-analysis of a frequentist trial, but rather the first analyses of the KALME trial outcomes will use Bayesian framework.

Simulation studies of the primary outcome within this new Bayesian framework demonstrated adequate preservation of the original operating characteristics of the KALME trial with respect to 80% power and 5% type 1 error (**Appendix 1**). This was demonstrated using 10,000 simulations of the trial conduct under the null and the postulated 35% reduction in opioid use, as well as a range of two other specifications, namely reduction of 40%, and increase in 35% in opioid use (**Figure 1** and **Appendix 1**), using the Core Adaptive Continuous Design Module within the Fixed and Adaptive Clinical Trial Simulator (FACTS) software (FACTS Development Team 2023).

Statistical analyses

All statistical analyses will be conducted on an intention–to–treat basis, with patients analysed according to their assigned treatment arms, except for cases lost to follow up or withdrawal of informed consent. No or minimal losses to follow–up for the primary outcome is anticipated. Complete–case analysis will be carried out for all the outcomes. However, if more than 5% of missing data is found for the primary outcome, a sensitivity analysis using multiple imputations will be carried out. Multiple imputation will consider imputation models based on prognostic baseline and post-baseline variables under a missing at random assumption. All analyses will be performed using R v.4.0.3.

As described above, KALME will consider a Bayesian analysis and all primary models described below will be adjusted only for location (site) as random effects. All Bayesian models will be fitted with the integrated nested Laplace approximation (INLA), allowing the calculation of posterior effect estimates with their 95% credible intervals (CrI), and the probability that ketamine is superior to placebo (efficacy). Prior distributions for individual treatment effects for all analyses described below will be

neutral (weakly informative). The criterion for declaring a most or least effective treatment will be a probability greater than 0.975. The threshold of 0.975 was chosen by convention (analogous to an alpha of 0.025 in a one-sided frequentist comparison).

The primary outcome will be analysed with Bayesian median regression model, which will calculate posterior probability distributions of median hourly dose of opioids used as an infusion, determined by fentanyl equivalents, and reported as μg/h (primary outcome) based on evidence accumulated in the trial and the prior probability distribution (the assumed previous knowledge). The median difference for the primary outcome will be modelled such that a value lower than 0 reflects a decrease in the median hourly dose of opioids in the ketamine group, implying benefit.

Other continuous outcomes will be analysed using the same model described for the primary outcome. Binary outcomes will be reported using a Bayesian logistic regression model reported as odds ratio with its 95% CrI. Time-to-event outcomes will be analysed using a Bayesian Cox proportional hazard model reported as hazard ratio with its 95% CrI. Free-days outcomes will be analysed using a Bayesian cumulative logistic model, reported as odds ratio with its 95% CrI, and with an odds ratio greater than 1 representing more free-days and implying benefit. There will be no planned adjustment for multiple comparisons of secondary outcomes, and results will be presented as the effect estimate with its 95% CrI, from which no conclusions can be drawn.

Confidentiality of patient data

The principal investigator will be responsible for data storage. Patients included in the study will be allocated a study number which will then be used in the database. Data

collected from ANZICS CORE will not include any identifiers. All data included in the study database will be de-identified.

Discussion

Patients who are admitted to ICU and require mechanical ventilation often require opioid medications to manage pain and aid with sedation (analgosedation). Opioid medications are associated with complications and therefore adjuncts should be sought. Ketamine seems an ideal agent to assist with analgosedation, as it possesses both analgesic and sedative properties, however data relating to its used in patients who are mechanically ventilated are lacking.

The KALME study aims to assess the effect of low dose ketamine infusion on hourly opioid use in fentanyl equivalents on patients receiving mechanical ventilation. Furthermore, it aims to assess the feasibility of, and inform, a larger multicentre randomised controlled trial of ketamine infusion for analgosedation.

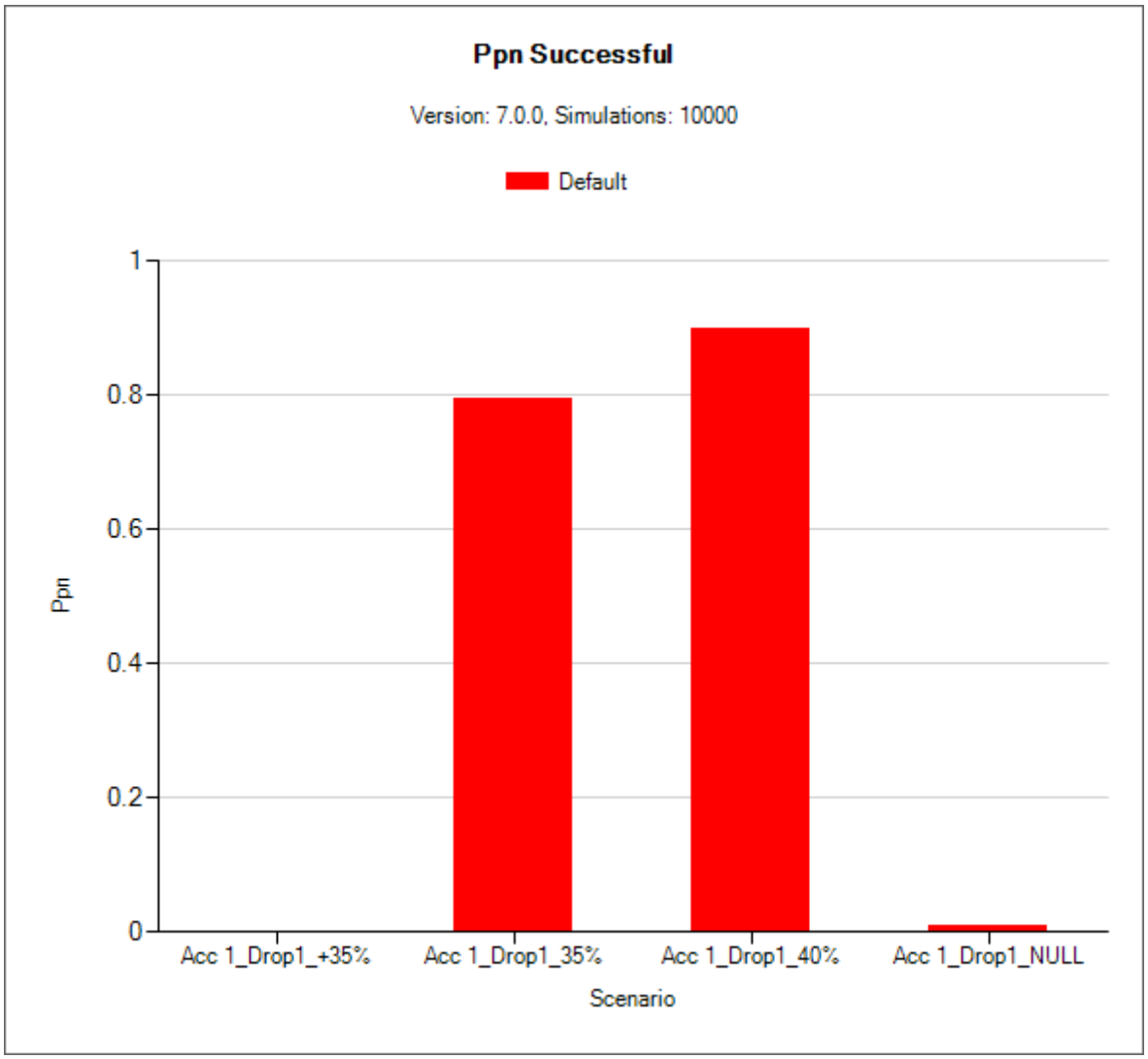
Funding

The KALME study received a grant of $47,900 from the AVANT Foundation and is also supported by the Austin Hospital Intensive Care Trust Fund.

Table 1 – Algorithm of Infusion

Weight range (kg)	Volume per hour infused (ml/hr)	Dose per hour infused (mg/hr)
40 - 49.9	**3.4**	**6.8**
50 - 59.9	**4.1**	**8.2**
60 - 69.9	**4.9**	**9.8**
70 - 79.9	**5.6**	**11.2**
80 - 89.9	**6.4**	**12.8**
90 - 99.9	**7.1**	**14.2**
≥ 100	**7.5**	**15**

Figure 1 – Probability of Success in Each of the Simulated Scenarios for the KALME Trial



Probability of success of each simulated scenario after 10,000 simulations considering an increase in the mean hourly opioid dose of 35% ('_+35%'), reductions in the mean hourly opioid dose of 35% ('_35%') and 40% ('_40%'), and the null scenario ('_NULL').

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APPENDIX 1

FACTS

Design and Simulation Report for the 'Ketamine for AnaLgesia in MEchanically Ventilated Adults' trial (KALME)

FACTS Core Engine for Continuous Endpoint

June 26, 2024

Table of Contents

This document describes the features of the simulated design, including the statistical models, decision rules, and simulation scenarios as input into the FACTS™ (Fixed and Adaptive Clinical Trial Simulator) software. A small set of operating characteristics for the simulations is also summarized.

This document defines the trial design that governs the overall conduct of the trial and the approach to analysis of the primary trial endpoint, i.e., the analysis that determines the overall interpretation of the trial outcome. The statistical approach to characterizing, presenting, and analyzing secondary and exploratory endpoints, and to the monitoring of safety outcomes will be contained within a separate Statistical Analysis Plan (SAP). The Design Report is not the Statistical Analysis Plan; rather it is a supplement to the SAP that contains design and primary analysis details. In addition, details of the clinical protocol, patient population, randomization, treatment, outcome assessments, and safety event monitoring are provided in the primary clinical trial protocol.

The primary endpoint is a continuous endpoint, measured at 1 weeks. Lower response corresponds to subject improvement.

The trial will enroll up to a maximum of 120 subjects, randomized among 2 arms, including a control arm and 1 treatment arms. We label these arms generically by their arm index as: $d = 0$ (Control), 1. We also denote by v_d the effective dose strength of each of the arms.

The arms in the trial are given as follows:

Table-1: Treatment Arms

Arm name	Arm strength v_d
Placebo	$v_0 = 0$
Ketamine	$v_1 = 1$

2. Statistical Modeling

This section describes the statistical modeling used in the design. The modeling is Bayesian in nature.

2.1. Final Endpoint Model

Let Y_i be the primary outcome measured at 1 weeks for the i^{th} subject. We model the outcomes as

$$Y_i \sim N\left(\theta_{d_i}, \sigma^2\right)$$

where θ_d is the mean response for arm d .

The mean response is modeled independently for each dose as:

$$\theta_0 \sim N(0, 10^2),$$

$$\theta_1 \sim N(0, 10^2).$$

Thus, θ_d for each dose is estimated separately using only data from that dose.

The error variance is modeled as:

$$\sigma^2 \sim IG(0.5{,}50),$$

where $\mathrm{IG}(a, b)$ is the inverse gamma distribution defined by:

$$f(x|a, b) = \frac{b^a e^{-b/x}}{x^{a+1}\Gamma(a)}.$$

2.2. Evaluation of Posterior Estimates

The Bayesian final endpoint model is fitted to the data at each update. The posterior is calculated as:

$$p(\omega|Y) \propto \prod_{i=1}^{n} p\left(y_i|\varphi\right)p(\varphi)$$

where φ is the set of parameters for the final endpoint model, $p(\varphi)$ is the prior for those parameters, y_i is the final response for each subject, and n is the number of subjects. The posterior is evaluated using MCMC with individual parameters updated by Metropolis Hastings (or Gibbs sampling where possible), using only the y_i data available at the time of the update.

2.3. Quantities of Interest

We define a number of quantities that will be tracked and may be used to make decisions during the trial.

2.3.1. Posterior Probabilities

For each dose, we calculate the following quantities from the posterior:

- the probability that the mean response on dose d is less than on Placebo by at least -1:

$$Pr(\theta_d - \theta_0 < -1)$$

- the probability that the mean response on dose d is less than on Placebo:

$$Pr(\theta_d < \theta_0)$$

2.3.2. Frequentist p-values

We test each active dose relative to control using a one-sided two-sample t-test $\theta_d < \theta_0$ and calculate the p-value where missing data is imputed using last observation carried forward (LOCF) and the analysis is unadjusted for multiple comparisons:

$$t\text{-test } p\text{-value (LOCF; unadjusted)}.$$

2.3.3. Predictive Probability of Future Trial Success

For each active dose, we calculate the predictive probability of success in a future trial. We assume a hypothetical trial with a fixed design that would equally randomize 500 subjects between control and one active dose (250 per arm). The final analysis would be a test of superiority . The predictive probability of future trial success is the chance of achieving statistical significance (one-sided $p < 0.025$) versus control if the active dose was entered into the hypothetical trial. This is different from the power for such a trial, in that the power calculations typically assume a fixed treatment effect, whereas the predictive probability of success averages over the posterior distribution of the treatment effect. Thus, knowledge of the treatment effect and the uncertainty in that knowledge are formally incorporated. We denote this probability as:

$$Pr(\text{Future Trial Success}; n = 250, \alpha = 0.025, \delta = 0).$$

2.3.4. Target Doses

We consider the following target doses:

- The maximum effective dose d_{max} is the dose with the greatest treatment effect (difference from control). For each dose, we calculate the probability of being the d_{max}:

$$Pr(Max).$$

- The minimally effective dose $MED_{\delta=-1}$ is the smallest dose that achieves at least a difference of $\delta = -1$ relative to control. We calculate the probability that each dose is the $MED_{\delta=-1}$:

$$Pr(MED_{\delta=-1} \text{ relative to control})$$

- The 90% effective dose $ED90$ is the smallest dose that achieves at least 90% of the treatment effect (relative to control) achieved by d_{max}. We calculate the probability that each dose is the $ED90$:

$$Pr(ED90 \text{ relative to control})$$

2.3.5. Decision Quantities

Throughout the trial, decisions may be based on the following quantities:

- Minimum t-test p-value (LOCF; unadjusted) across all doses
- Maximum $Pr(\theta_d < \theta_0)$ across all doses

2.4. Conventions for Missing Data

At any analysis, some participants may have missing data for the final endpoint. The missing data could result from the participant dropping out of the study, the participant is on an arm that has been dropped or because the participant simply has not yet reached the final visit.

If at the time of the final analysis the participant has no final visit data due to dropping out, no final endpoint value is imputed for the participant.

Any p-value Quantity of Interest has a specified rule for the treatment of missing data, this rule is applied to all participants with no final visit data, whatever the cause.

3. Study Design

3.1. Timing of Interim Analyses

This is a fixed trial. No interims have been specified.

3.2. Allocation

The trial will enroll 120 subjects that will be randomized to the treament arms in a fixed ratio. Randomization will occur in blocks of size 2, with ratio of 1:1 within each block.

3.3. Criteria for Stopping Accrual

3.3.1. Stopping for Futility

If a futility stopping rule is met at an interim analysis, then subject follow up will be discontinued, and the final evaluation criteria will be applied to the currently available data.

3.3.2. Stopping for Expected Success

If a success stopping rule is met at an interim analysis, then a final analysis will be conducted after all currently enrolled subjects have been followed to their final endpoint.

3.4. Final Evaluation Criteria

At the final analysis, the trial will be considered futile if any of the following criteria are satisfied:

- Maximum $Pr(\theta_d < \theta_0)$ across all doses < 0.975

At the final analysis, the trial will be considered successful if all of the following criteria are satisfied:

- Maximum $Pr(\theta_d < \theta_0)$ across all doses > 0.975

4. Simulation Scenarios

We evaluate the proposed design through trial simulation. We hypothesize several possible underlying truths for the mean response, as well as for trial execution variables such as accrual and dropout. For each of these scenarios, we generate data according to those truths and run through the design as specified above. We repeat this process to create multiple ``virtual trials" and we track the behavior of each trial. In this section, we describe the the parameters used to generate the virtual subject-level data.

4.1. Virtual Subject Response Profiles

We consider 4 profiles for which subject outcomes for the final endpoint are simulated to have means as shown in Table-2 and standard deviations shown in Table-3.

Table-2: Virtual subject response means

VSR	d_0	d_1
+35%	67	90.45
35%	67	43.55
40%	67	40.2
NULL	67	67

Table-3: Virtual subject standard deviations

VSR	d_0	d_1
+35%	39	39
35%	39	39
40%	39	39
NULL	39	39

4.2. Accrual Profiles

We simulate the random arrival of subjects into the trial from a Poisson process with the mean weekly rates specified in Table-4. Within each accrual profile, there may be differential recruitment rates over time and across regions. Thus for each region, we specify:

- the mean number of subjects per week at peak accrual,
- the start date (in weeks from the start of the trial),
- whether the region will have a ramp up phase, and if so, when the ramp up will be complete, and
- whether the region will have a ramp down phase, and if so, when the ramp down will begin and when it will be complete.

Ramp up and ramp down define simple linear increases and decreases in the mean recruitment rate from the start to the end of the ramp. Thus some simulated trials recruit more quickly than this and some more slowly.

Table-4: Accrual Profiles

Profile Name	Region Index	Peak Rate	Start Week	Ramp Up	Ramp up Complete	Average Accrual Completion
Acc 1	1	5	0	Yes	10	30

4.3. Dropout Profiles

We simulate subjects dropping out of the trial with the rates (per dose and visit) shown in Table-5.

Table-5: Dropout Profiles

Profile	Week	d_0	d_1
Drop1	1	0.05	0.05

5. Operating Characteristics

For the scenarios described above, we simulate multiple virtual trials and track the behavior of each trial, including the final outcome of the trial, the estimated mean response, etc. The results in this section are summarized across all simulated trials for each scenario.

5.1. Overall

This section gives a high-level description of the operating characteristics. Table-6 shows the following information per scenario:

- N sim: the number of simulated trials
- E[N]: the expected sample size
- Pr(success): the proportion of trials that met the final success criteria
- E[duration]: the expected duration of the trial in weeks.

Table-6: Overall Operating Characteristics

Accrual	Dropout	VSR	N sim	E[N]	Pr(Success)	E[duration]
Acc 1	Drop1	+35%	10000	120	0.0000	30.5
Acc 1	Drop1	35%	10000	120	0.7946	30.5
Acc 1	Drop1	40%	10000	120	0.8973	30.5
Acc 1	Drop1	NULL	10000	120	0.0086	30.5

5.2. Trial Outcomes

This section summarizes the outcomes of the simulated trials. For each scenario in Table-7, the columns represent the proportion of simulated trials meeting each of the following definitions:

- Late Success (LS): enrolled to the maximum sample size and successful at the final analysis
- Late Futility (LF): enrolled to the maximum sample size and met the futility criteria at the final analysis

Table-7: Trial Outcomes

Accrual	Dropout	VSR	LS	LF
Acc 1	Drop1	+35%	0.0000	1.0000
Acc 1	Drop1	35%	0.7946	0.2054
Acc 1	Drop1	40%	0.8973	0.1027
Acc 1	Drop1	NULL	0.0086	0.9914

6. Computational Details

This report reflects the design parameters contained within the `KALME.facts` file. The simulations were run using FACTS (Berry Consultants, LLC, Austin, TX) version 7.0.0. Table-8 shows the computational details for each scenario, including the starting date and time, the length of the MCMC chain, the random number seed, and the trial at which the simulation started. The R software package was used to summarize the simulation output and to create tables for this report.

Table-8: Computational Details

Accrual	Dropout	VSR	Date Time	MCMC Burn-in	MCMC Length	Random Seed	Starting Trial
Acc 1	Drop1	+35%	06/26/2024 09:42:47	1000	2500	3500	1
Acc 1	Drop1	35%	06/26/2024 09:42:47	1000	2500	3500	1
Acc 1	Drop1	40%	06/26/2024 09:42:47	1000	2500	3500	1
Acc 1	Drop1	NULL	06/26/2024 09:42:47	1000	2500	3500	1