The Intensive Care Platform Trial (INCEPT)

INCEPT-Albumin synopsis

Domain-specific appendix version and date
Version 1.4, 2025-08-20

Corresponding core protocol version and date
Version 1.4, 2025-08-20

Applicable core protocol registration numbers
European Union Clinical Trials Information System (CTIS) EUCT number: 2024-516208-41-00.
ClinicalTrials.gov identifier: NCT06667999.
Universal Trial Number: U1111-1313-8171.

Websites
www.incept.dk

www.incept.dk/albumin

Protocol synopsis

Background
Use of intravenous albumin is suggested for certain types of shock if patients have received large volumes of crystalloids. This recommendation is primarily based on moderate certainty of evidence for positive effects of albumin on short-term circulatory endpoints. Albumin is also used for substitution, as hypoalbuminemia is frequent in critical illness and associated with poor outcomes. Yet, the clinical use of albumin varies markedly. At present it is uncertain if the potential desirable circulatory effects of albumin translate into patient benefits in adult intensive care unit (ICU) patients with shock.

Objectives
We aim to assess the effects of albumin for resuscitation and substitution therapy versus no use of albumin on the number of days alive without life support at 30 days and other patient-important outcomes in adult ICU patients with shock. We hypothesise that the use of albumin may result in more days alive without life support at 30 days.

Design
The albumin versus no albumin in shock (INCEPT-Albumin) domain will be an investigator-initiated, open-label domain with an integrated feasibility phase on the pragmatic, parallel-group, randomised embedded, multifactorial, international, adaptive Intensive Care Platform Trial (INCEPT). The domain will employ adaptive stopping for superiority/inferiority and practical equivalence and restricted response-adaptive randomisation.

Inclusion and exclusion criteria
Adult acutely admitted ICU patients will be screened for the INCEPT-Albumin domain if both interventions are considered clinically appropriate and they have shock irrespective of cause. We will exclude patients for whom legal consent is expected to be unobtainable, patients under coercive measures, patients who have received albumin during the current ICU stay, patients with traumatic brain injury, pregnant patients, patients with known religious objection to albumin, patients with known albumin allergy, and patients who are included in another interventional trial or *INCEPT* domain where co-enrolment with *INCEPT-Albumin* is not permitted.

Interventions and comparisons
The intervention period is from time of randomisation to a maximum of 90 days in the ICU. If participants are transferred or readmitted to a participating ICU during this period, the assigned intervention will continue.

Albumin use in the ICU (intervention)
Albumin should be used for the following indications:

- During circulatory failure in addition to crystalloids (resuscitation)
- For substitution in case of:
    - Suspected or overt albumin loss
    - P-albumin levels ≤25 g/L

No albumin use in the ICU (control)
Albumin should not be used.
In case of the following special circumstances, albumin may be considered:

- Large ascites drainage (i.e., >1L tapped)
- Spontaneous bacterial peritonitis
- Hepatorenal syndrome

Outcomes
The primary outcome guiding all adaptations is days alive without life support at day 30 (non-survivors will be assigned 0 days). Additional outcomes will be the remaining core outcomes in INCEPT: all-cause 30-, 90-, and 180- day mortality, days alive without life support at day 90; days alive out of hospital at day 30 and 90; days free of delirium at day 30; health-related quality of life (HRQoL; evaluated using EQ-5D-5L index values and EQ VAS) and cognitive function (evaluated using the Montreal Cognitive Assessment test 5-minute version [Mini MoCA]) at 180 days); and one or more domain-specific safety outcomes including serious adverse reactions (severe anaphylactic reactions and major bleeding) and suspected unexpected serious adverse reactions at day 30 and 90.

Statistics and adaptation rules
This domain will use Bayesian statistical methods with neutral, weakly informative priors conducted in the intention-to-treat population (primary analyses). Adaptive analyses will be conducted after follow-up and data collection for the first 1,000 participants and every subsequent 250 participants up to a maximum of 10,000 participants.
The domain will use constant, symmetrical stopping rules for superiority/inferiority calibrated to keep the type 1 error rate at 5%. The domain will be stopped for practical equivalence if there is >90% probability that the absolute mean difference between arms is less than 1 day.
Equal initial allocation will be used followed by response-adaptive randomisation with minimum allocation probabilities of 40% to each arm.

Domain design performance metrics
Performance metrics have been evaluated assuming a mean of 14.5 days alive without life support in the control arm (*no albumin use*) and scenarios with no, small, and large differences between arms corresponding to 0 days, 1 day and 5 days in either direction in different combinations. The expected (mean) sample sizes under these scenarios range from 1,137 to 3,547 participants. The probabilities of conclusiveness (i.e., superiority/inferiority or equivalence) are ~100% in all scenarios, and the probabilities of superiority (power) range from 59% to ~100% in the scenarios with differences between arms.

Estimated timeline

- First quarter, 2025: domain approved
- Second quarter, 2025: first participant randomised
- Second quarter, 2026: feasibility phase analysis concluded

- Fourth quarter, 2028: expected inclusion of the last participant if the domain continues to the expected sample size in the small-difference scenario (i.e., the largest expected sample size under the different scenarios assessed)
- Second quarter, 2034: expected inclusion of the last participant if the domain continues to the maximum sample size (n = 10,000); the probability for this is very low
- Approximately 5 months after inclusion of the last participant: primary report on 30- and 90-day outcomes submitted
- Approximately 9 months after inclusion of the last participant: report on 180-day outcomes submitted

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