Synopsis CRYSTALLBrain

Status	Genehmigt

Organisation	Insel Gruppe
Kürzel	-

Version	2.1.0
Gültig ab	14.10.2024

Autoren	Anna Messmer, Leitung CRYSTALLBrain, Freigabe am 14. Oktober 2024
Review	-
Genehmigung	Carmen Pfortmüller, Leitung UK-Intensivmedizin-Forschung, Freigabe am 14. Oktober 2024

Anmerkung

Das vorliegende Dokument ist eine Kopie aus der Applikation «Orca». Das Original, respektive die aktuell gültige Version ist unter orca.dkfbasel.ch verfügbar.

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Dokument e69eaa5f-8a21-11ef-89cc-0242ac120005
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Änderungsverzeichnis

Version	Beschreibung
Version: 2.1.0 (aktuell)	neu in ORCA

Appendix 01

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Crystalloid Fluid Choice and Neurological Outcome in Patients after Subarachnoid Haemorrhage – a multi-center randomized double-blind clinical trial (CrystallBrain)

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Study Type:	Investigator-initiated clinical trial, comparison of two already established treatment protocols
Study Categorisation:	A
Study Registration:	Clinicaltrials.gov (NCT04043598)
Study Identifier:	CrystallBrain
Sponsor	Prof. Dr.med. Carmen Andrea Pfortmueller, Department of Intensive Care Inselspital, Bern University Hospital and University of Bern Freiburgstrasse 10 3010 Bern
Principal and Coordinating Investigator:	Dr.med. Anna Sarah Messmer Department of Intensive Care Inselspital, Bern University Hospital and University of Bern Freiburgstrasse 10 3010 Bern
Investigational Product:	0.9% saline (Bichsel, Interlaken, Switzerland) versus Ringer`s lactate (Bichsel, Interlaken, Switzerland)
Protocol Version and Date:	27.12.2023 V2.1

STUDY SYNOPSIS

Sponsor / Sponsor-Investigator	Prof. Dr. med. Carmen A. Pfortmueller PI und CI (coordinating investigator): Prof. Dr.med. Carmen Andrea Pfortmueller
Study Title:	Crystalloid Fluid Choice and Neurological Outcome in Patients after Subarachnoid Haemorrhage – a randomized double-blind clinical trial (CrystallBrain)
Short Title / Study ID:	CrystallBrain
Protocol Version and Date:	Version 2.1, 27.12.2023
Trial registration:	Clinicaltrials.gov, NCT04043598
Study category and Rationale	A Investigator-initiated clinical trial of two already established treatment protocols
Clinical Phase:	Phase 4, observational trial
Background and Rationale:	Despite ongoing advances in critical care, mortality and morbidity of patients with subarachnoid haemorrhage remains high. Secondary brain injuries related to cerebral vasospasm and consecutive ischemic brain injury and intracerebral edema are considered the main contributors to mortality and morbidity in these patients. Evidence points towards low serum sodium levels being one of the risk factors for secondary brain injury in this patient population. Previous studies show that fluid resuscitation with normal saline results in higher serum sodium levels and higher serum osmolality when compared to balanced infusates. It therefore seems probable that use of saline (0.9%) in these patients might improve outcome.
Objective(s):	The primary objective of this study is to evaluate whether the use of saline (0.9%) results in less clinically important vasospams compared to lactated Ringer`s in patients with subarachnoid haemorrhage.
Outcome(s):	The primary endpoint will be the occurrence of clinically relevant vasospasms defined as new neurologic deficit requiring immediate intervention.
Study design:	Multi-center investigator-initiated randomized-controlled double blind clinical trial comparing to already established treatment protocols.

Inclusion / Exclusion criteria:	Participants fulfilling all of the following inclusion criteria are eligible for the study: Patients suffering from presumed non-traumatic subarachnoid haemorrhage (SAH) admitted to our institution. The presence of any one of the following exclusion criteria will lead to exclusion of the participant: - Patient with intra-cranial trauma - Diagnosis of an AV-malformation as the source of subarachnoid haemorrhage on the primary CT/MRI or angiography if performed prior to randomisation - > 24 hours since first diagnosis of SAH (as diagnosed by cerebral imaging (CT or MRI) - Patients with established limitation of therapy at hospital admission (e.g. ICU admission for evaluation of organ donation)
Measurements and procedures:	All patients admitted to the Bern University Hospital with the diagnosis of intracerebral haemorrhage will be screened and if eligible, randomized to one of the study arms. Thereafter, patients will receive exclusively the allocated study fluid for fluid maintenance and resuscitation from study inclusion until ICU/intermediate care (IMC) discharge. Thereafter, patients will be followed for evaluation of secondary endpoints.
Study Product / Intervention:	We will compare 0.9% saline (Bichsel) to Ringer`s lactate (Bichsel) in respect to outcome in patients with subarachnoid haemorrhage.
Control Intervention (if applicable):	NA
Number of Participants with Rationale:	Sample size calculation based on our registry data revealed a size of 160 patients per group to be necessary to find a 15% difference in neurological outcome. Therefore, we will include 320 patients under estimation of a 15% dropout rate.
Study Duration:	May 2022 to April 30th 2025
Study Schedule:	Start: May 24th 2022 Active study end: December 31st 2024 Last patient out: June 30th 2025

Investigator(s):	Anna S. Messmer MD[1], Stephan Jakob MD[1], Werner Z`Graggen MD[1,2], Joerg C. Schefold MD[1], Carmen A. Pfortmueller MD[1] [1] Department of Intensive Care, Inselspital, Bern University Hospital and University of Bern, Bern, Switzerland [2] Department of Neurosurgery, Inselspital, Bern University Hospital and University of Bern, Bern, Switzerland
Study Centre(s):	Department of Intensive Care Medicineand Department of Neurosurgery, Inselspital Bern University Hospital, Bern, Switzerland Department of Intensive Care Medicine, University Hospital Geneva (HUG), Geneva, Switzerland
Statistical Considerations:	Whether the use of normal saline significantly influences our primary endpoint will be assessed by using Chi-Square test. Our secondary endpoints will also be assessed by Chi-Square test with exception of the mRS, GOSE and miniMOCA assessment which will be assessed by Wilcoxon rank sum test. In the event of an uneven baseline situation, multivariable regression (linear regression for interval outcomes and logistic regression for dichotomous outcomes) will be used for adjustment of baseline differences.
GCP Statement:	This study will be conducted in compliance with the protocol, the current version of the Declaration of Helsinki, the ICH-GCP or ISO EN 14155 (as far as applicable) as well as all national legal and regulatory requirements.