1. TITLE PAGE

Study title

Prospective, controlled, single-blind, bicentric, randomized study on the safety of HES 130/0.42 combined with a balanced electrolyte solution vs. 5% albumin combined with an unbalanced electrolyte solution (NaCl 0.9%) in patients with compensated renal failure

Name of test drug / investigational product

Tetraspan® 6%

Indication studied

Perioperative plasma volume replacement in patients with compromised renal function defined by a serum creatinine level between 1.5 mg/dL and 3.0 mg/dL.

Study design

Prospective, controlled, single-blind, bicentric, randomized study performed in two parallel groups

Sponsor

B. Braun Melsungen AG
Division Hospital Care
Carl-Braun-Straße 1
34212 Melsungen, Germany

Study number

HC-G-H-0514

Development phase of study

Phase IV

Study initiation date

First patient in : 06 November 2009

Study completion date

Last patient out : 17 June 2010

Coordinating investigator (Leiter der klinischen Prüfung according to German Drug Law)

Prof. Dr. med. Thomas Lücke
Ruprecht-Karls-Universität Heidelberg
Medizinische Fakultät Mannheim
Klinik für Anästhesiologie und operative Intensivmedizin
Theodor-Kutzer-Ufer 1 – 3
68167 Mannheim, Germany
Phone ++49-(0)621 / 383-3155
Fax ++49-(0)621 / 383-2021
eMail thomas.luecke@anaes.ma.uni-heidelberg.de

Study coordinator	[redacted] Scientific Manager Hospital Care Division B. Braun Melsungen AG Carl-Braun-Straße 1 34212 Melsungen, Germany Phone ++49-(0)5661 / 71-[redacted] Fax ++49-(0)5661 / 75[redacted] eMail [redacted]@bbraun.com
GCP	This study was performed in compliance with ICH Good Clinical Practice (CPMP/ICH/135/95).
Date of the report	23 August 2011

2. SYNOPSIS

Name of Sponsor	B. Braun Melsungen AG, Carl-Braun-Straße 1, 34212 Melsungen, Germany
Name of finished product	Tetraspan® 6%
Name of active ingredient	Hydroxyethyl starch (6% HES 130/0.42)
Study title	Prospective, controlled, single-blind, bicentric, randomized study on the safety of HES 130/0.42 combined with a balanced electrolyte solution vs. 5% albumin combined with an unbalanced electrolyte solution (NaCl 0.9%) in patients with compensated renal failure
Investigators	• Coordinating investigator: – *Mannheim* – Prof. Dr. med. Thomas Lücke Ruprecht-Karls-Universität Heidelberg Medizinische Fakultät Mannheim Klinik für Anästhesiologie und operative Intensivmedizin Theodor-Kutzer-Ufer 1 – 3 68167 Mannheim, Germany • Principal investigator: – *Ludwigshafen* – [redacted] c/o Klinikum der Stadt Ludwigshafen gGmbH Klinik für Anästhesiologie und operative Intensivmedizin Bremserstraße 79 67063 Ludwigshafen am Rhein, Germany
Study centers	2 centers in Germany
Publication (reference)	–
Study period	Date of first patient enrolled: 06 November 2009 Date of last patient completed: 17 June 2010.
Phase of development	IV
Objectives	Impact of two different volume replacement therapy regimes on base excess in patients with reduced renal function (creatinine > 1.5 mg/dL and < 3.0 mg/dL). Investigation of safety and efficacy of a balanced and an unbalanced volume replacement regime: Renal function, hemodynamics, blood losses, amount of given blood products (RBC, platelets, FFP), electrolytes, outcome and other data like concomitant medication.
Methodology	Prospective, controlled, single-blind, bicentric, randomized study performed in two parallel groups.
Number of patients	• Planned: N= 52 • Screened: N= 2 • Randomized: N= 2 • Completers of perioperative study phase: N= 2 • Completers of follow-up phase: N= 1.
Diagnosis and criteria for inclusion	Perioperative plasma volume replacement in patients with compromised renal function defined by a serum creatinine level between 1.5 mg/dL and 3.0 mg/dL.
Test product	Tetraspan® 6% combined with a balanced electrolyte solution (Sterofundin® ISO)
Dose	Maximum daily dose 50 mL HES/kg body weight (equivalent to 3.0 g HES/kg body weight).
Mode of administration	Intravenous application
Batch no.	Tetraspan (HES): 9125H51 + Sterofundin ISO: 9124A243

Duration of treatment	Depending on the duration and degree of hypovolemia.
Reference product	Human Albumin 50g/L Baxter combined with an unbalanced electrolyte solution (NaCl 0.9%)
Dose	According to the needs of the individual patients for the treatment of hypovolemia and the achievement of hemodynamic stability.
Mode of administration	Intravenous application
Batch no.	Human Albumin 50g/L Baxter: VNA1H104 + NaCl 0.9%: 9141A214
Criteria for evaluation	
Primary endpoint	Course of base excess from pre-anesthesia until immediately after surgery.
Secondary endpoints	Efficacy Hemodynamic parameters • systolic arterial pressure (SAP) [mmHg] • diastolic arterial pressure (DAP) [mmHg] • mean arterial pressure (MAP) [mmHg] • heart rate (HR) [beats/min] • central venous pressure (CVP) [mmHg] • positive end-expiratory pressure (PEEP) [cmH_2O]. Safety • renal function • blood gas analysis • electrolytes • post-operative nausea and vomiting (PONV) • need of hospital dialysis.
Statistical methods	Statistical estimates will not be used.

SUMMARY – CONCLUSION

Safety results

Only two patients entered and terminated the perioperative study phase. Both cases were treated with Human Albumin 50 g/L Baxter + NaCl.

Serious adverse events did not occur. Adverse events were reported in one patient: mild hypovolemia not requiring any action; causality: unlikely; outcome: the event resolved without sequelae.

The base excess decreased in both patients by 4.3 and 4.5 mmol/L, respectively. The same tendencies of further parameters were observed for

- pH, Hb, Hct, HCO_3^-, Ca: decrease
- pO_2, Na, K, Cl : increase.

A PONV was not observed, and a hospital dialysis was not necessary.

Efficacy results

The hemodynamic parameters showed no marked deviations from normal.

CONCLUSION

In both patients, Human Albumin 50 g/L Baxter + NaCl was well tolerated. No adverse events related to the IMP were observed. Serious adverse events were not reported. The hemodynamic parameters showed no marked deviations from normal. The base excess decreased in both patients by > 4.0 mmol/L.