Clinical Study Report for Investigational Medicinal Product SKNt-001-CP4 SmofKabiven® extra Nitrogen

SYNOPSIS

Name of Sponsor/Company: Fresenius Kabi Deutschland GmbH Else-Kröner-Straße 1 D-61352 Bad Homburg, Germany	Individual Study Table Referring to Part of the Dossier (For National Authority use only) Volume: Page:
Name of Finished Product: SmofKabiven® extra Nitrogen	
Name of Active Ingredients: Amino acids, glucose, lipids, and electrolytes	

Title of Study:
Reaching Protein Target with SmofKabiven® extra Nitrogen Versus Olimel N9E: A Prospective, Randomised, Active-controlled, Patient-blinded, Multicentre Clinical Trial During the Early Phase of Acute Critical Illness

Fresenius Study Identifier: SKNt-001-CP4

EudraCT number: 2017-001972-46

Countries involved in the study:
The study was planned to be performed in France, Germany, and Poland; patients were only enrolled in France.

Investigators:	Coordinating Investigator (CI) and National CI for France:	Pr Julien Bohé, M.D., Ph.D. Service de Réanimation Unité de recherche clinique Soins critiques, France
	National CI for Germany:	Prof. Dr. med. Stefan Schaller Klinik für Anästhesiologie mit Schwerpunkt operative Intensivmedizin Charité Universitätsmedizin Berlin, Germany
	National CI for Poland:	Dr. Bernard Zajac Wojewódzki Szpital Specjalistyczny we Wrocławiu Oddział Anestezjologii i Intensywnej Terapii Wrocław, Poland

Publication (reference):	No study data has been published yet.
Studied period:	26 November 2019 (first patient enrolled) to 24 March 2020 (last patient completed).

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Phase of development:	4
Objectives:	To explore the efficacy of SmofKabiven® extra Nitrogen compared with Olimel N9E in reducing the cumulative protein deficit with the same caloric target during the early phase of acute critical illness in haemodynamically stable adult patients who required PN.
Methodology:	This was a prospective, randomised, patient-blinded, parallel-group, active-controlled, multicentre study in haemodynamically stable critically ill adults requiring PN.
Number of patients (planned and analysed):	120 patients planned; 7 patients enrolled; 0 patients withdrawn; 6 subjects analysed for safety. From March 2020 onwards the coronavirus disease 2019 (COVID-19) pandemic reached Europe and became the sites' focus and screening activities for this study were stopped. A temporary recruitment halt was announced on 09 April 2020 since hospitals would no longer allow monitors to enter the sites. On 07 September 2020 after 6 months of recruitment this study was terminated.
Diagnosis and main criteria for inclusion:	Haemodynamically stable, critically ill male and female patients, aged 18 to 90 years with a Body Mass Index (BMI) of 18.5 to 35 kg/m^2.
Test product, dose and mode of administration, batch number:	SmofKabiven® extra Nitrogen was infused via central venous access at a constant rate over 24 hours on 5 consecutive treatment days. The caloric target of 20 kcal/kg/day was provided with 22.48 mL/kg/day, which contained 1.5 g/kg/day of amino acids.

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	SmofKabiven® extra Nitrogen batch number used: 10MH7324 – expiry 08/2020.
Standardised EN product:	Fresubin® Original was administered as a standard product for EN in both treatment arms at the investigator´s discretion and according to the protocol. 2 Fresubin® Original batch numbers were used: 29NC0692 and 29NC0696 – both with an expiry 06/2020.
Duration of treatment:	5 days
Reference therapy, dose and mode of administration, batch number:	Olimel N9E (manufactured by Baxter) was infused via central venous access at a constant rate over 24 hours on 5 consecutive treatment days. The caloric target of 20 kcal/kg/day was provided with 18.69 mL/kg/day, which contained 1.07 g/kg/day of amino acids. Olimel N9E batch number used: 18F12N22 – exp. 05/2020.
Criteria for evaluation **Safety:** **Efficacy:**	Due to the low number of patients and event counts, no summary statistics were prepared. Adverse events, vital signs and laboratory parameters for each patient were assessed. No efficacy parameters were examined in this study.
Statistical methods:	Due to premature termination of the study, limited data were available only. Therefore, the analysis performed was on safety only. Individual data listings were prepared with data from all 6 randomised patients, but no statistical analysis was performed.
Summary – conclusions Safety results:	A total of 6 patients were treated with the study drug for up to 5 days. 3 of the 6 patients received SmofKabiven® extra Nitrogen, 1 patient received 100 % of the daily caloric target on

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5 treatment days, 1 patient received between 61 % and 79 % of the daily target on 5 treatment days, and another patient received 95 % and 97 % of the daily target on 2 consecutive treatment days. Of the 2 patients who received Olimel N9E only, 1 patient received 100 % of the daily target on 5 treatment days and another patient received between 85 % and 100 % of the daily target on 4 treatment days. One patient first received Olimel N9E for 2 days in accordance with random assignment to this study drug but was then erroneously treated with SmofKabiven® extra Nitrogen for the following 2 days. The patient received 100 % of the daily target on all 4 treatment days.

Overall, 4 patients (66.7 %) experienced a total of 23 treatment-emergent adverse events (TEAE) during the study, including all patients in the SmofKabiven® extra Nitrogen group (100 %) and the single patient who received both SmofKabiven® extra Nitrogen and Olimel N9E. No TEAEs were reported in the 2 patients who received Olimel N9E only.

Metabolism and nutrition disorders was the system organ class with the highest number of patients affected (7 events in 3 patients), followed by gastrointestinal disorders (3 events in 2 patients), cardiac disorders, and general disorders and administration site conditions (2 events in 2 patients each).

One TEAE in a patient treated with SmofKabiven® extra Nitrogen only was considered related to the study drug by the investigator (mild refeeding syndrome started on day 3 of study treatment and resolved at the end of the 5-day study treatment). This case occurred in an 82-year-old female patient with a baseline body weight of 63 kg and a body mass index of 25.5

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	who received 100 % of daily target study drug intake on all 5 treatment days without calories from other sources. The TEAE severity was mild in 10 cases, moderate in 6 cases, severe in 6 cases, and fatal in 1 case. None of the severe TEAEs were considered related to the study drug by the investigator. Three TEAEs in 2 patients who received SmofKabiven® extra Nitrogen were considered serious. None of them were considered related to the study drug by the investigator. Of these 3 events, 2 events in 1 patient resolved, while 1 event in another patient was fatal. The death was considered unrelated to the study drug. Laboratory measurements and vital signs were in line with expected values for critically ill patients.
Conclusion:	The study was prematurely terminated due to low recruitment in the context of the COVID-19 pandemic, with only 6 patients randomly assigned to study drug. The termination of the study did not allow any conclusions on the efficacy of the therapy with the study drug. Safety data available for patients completing this study did not indicate any safety concerns with the investigational product.