SYNOPSIS

Title of the study:	A Double-Blind, Randomized, Placebo-Controlled Multicenter Study Evaluating the Efficacy and Safety of two doses of Satavaptan (SR121463B) Versus Placebo in Patients with Dilutional Hyponatremia due to the Syndrome of Inappropriate Antidiuretic Hormone Secretion (SIADH) (EFC10102)
Investigator(s):	The 2 patients enrolled in the study were from 2 centers (both in the US). No principal investigator was identified for this study.
Study center(s):	There were 19 centers (in 5 countries) initiated.
Publications (reference):	None
Study period:	
Date first patient enrolled:	14 October 2008
Date last patient completed:	10 December 2008
Phase of development:	Phase 3

Objectives:

The objectives of this study were:

Primary: To assess the efficacy of satavaptan 10 and 25 mg/day versus placebo in correcting hyponatremia at Day 5 (predose) in patients with dilutional hyponatremia due to SIADH.

Secondary: To assess the safety of satavaptan versus placebo, as well as the maintenance of corrected serum sodium, the clinical outcome, quality of life, and health economic parameters in patients treated with satavaptan at Days 5 and 30.

The study was stopped prematurely as the result of the Sponsor's decision. Consequently very limited data were collected for the 2 patients randomized, and no analyses were performed. The data which are presented in this synopsis report are also supported by limited appendices.

Methodology:

This was a double-blind, randomized, placebo-controlled, multicenter, parallel group study with a 30-day treatment phase. Subjects who were eligible for the study were to be randomly assigned to the satavaptan 10 mg/day, satavaptan 25 mg/day or placebo group for the initial 4 days of the treatment period. For Days 5 – 11 all patients randomized to satavaptan treatment groups were to be combined in one group receiving the 10 mg dose whereas the patients randomized to the placebo group were to continue to receive placebo. For Day 12 up to the end of the treatment period at Day 30 the study treatment dose could be adjusted in the range of 10 to 25 mg satavaptan or matching placebo based on an individual benefit/risk evaluation.

It was planned that a Data Safety Monitoring Board would review the data from this study as part of the general review for the compound. However, the study was stopped prematurely and no data from this study were reviewed by the board.

Number of patients: Planned: 129 Randomized: 2 Treated: 2 Safety : 2

Diagnosis and criteria for inclusion:

Patients with SIADH of any origin with serum sodium between 115 and 132 mmol/L on 2 consecutive measurements at least 24h apart before randomization (screening and baseline), were included in this study.

Investigational product: satavaptan (SR121463B) tablets

Dose: 5 mg or 25 mg tablets

Administration: Oral administration in the morning

Batch number(s): [redacted]

Duration of treatment: 30 days

Duration of observation: 67 days (including a screening phase, a treatment phase, and a post-treatment follow-up phase)

Reference therapy: Placebo tablets

Dose: NA

Administration: Oral administration in the morning

Batch number(s): [redacted]

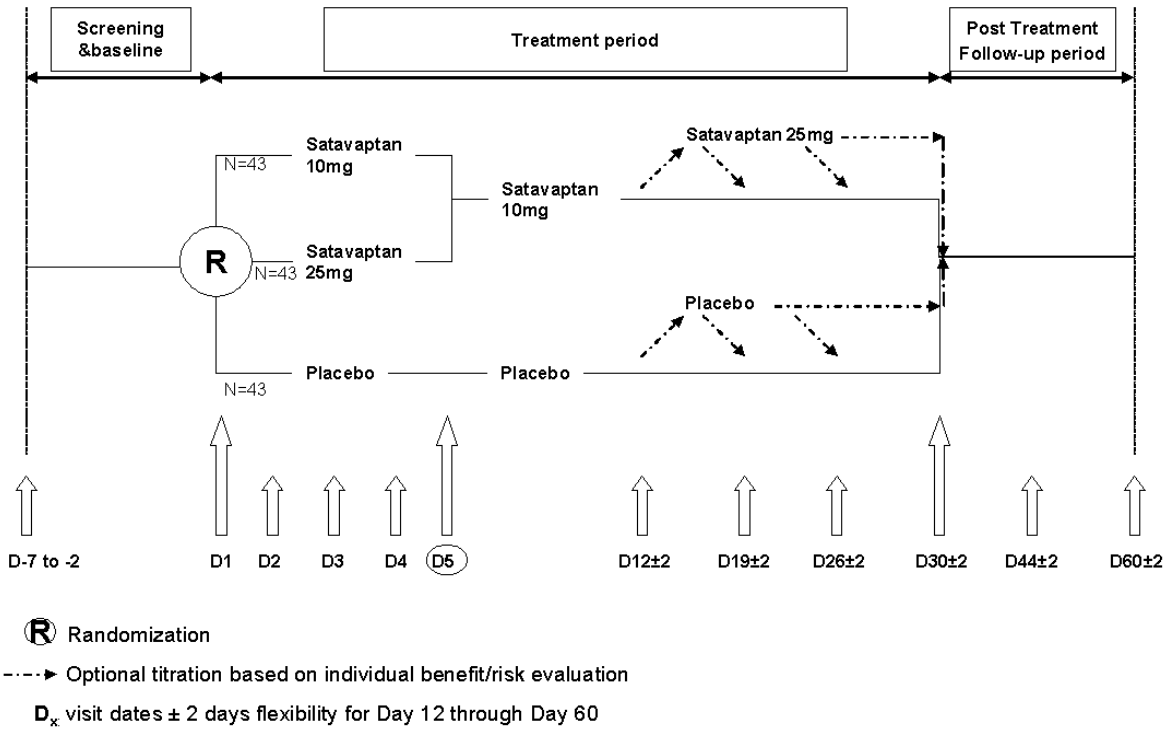
Criteria for evaluation: Due to limitations of the data collected during the study, only a summary of the relevant safety data for each individual patient will be provided. No other criteria were evaluated.

Statistical methods: No statistical analyses of the data were performed

Summary:

A summary of the study design is provided below, and a study flow chart is provided at the end of the document.

Figure 1 – Graphical study design



Patient demographics, patients and exposure:

Two Caucasian female patients, aged 51 and 52 years old respectively, were randomized. Both patients prematurely stopped the study as the result of the Sponsor's request.

As shown in the table below, both patients received satavaptan, 10 or 25 mg, for approximately 3 weeks.

Table 1 – Summary of exposure to study drug for the two patients included

Subject	Treatment (dose)	First intake	Last intake
A	satavaptan (10mg) satavaptan (25 mg)	27-Oct-2008 (D1) 07-Nov-2008 (D12)	06-Nov-2008 (D11) 12-Nov-2008 (D17)
B	satavaptan (25 mg) satavaptan (25 mg) satavaptan (25 mg)	20-Oct-2008 (D1) 29-Oct-2008 (D10) 07-Nov-2008 (D19)	28-Oct-2008 (D9) 06-Nov-2008 (D18) 11-Nov-2008 (D23)

Safety results:

There were no deaths, serious adverse events, or adverse events (AEs) leading to discontinuation during the study. A complete summary of AEs by system organ class and preferred term is provided in the following table.

Table 2 – Summary of all adverse events (pre-, on- and post-treatment) for the two patients included

Subject	AE classification	SOC	PT	Intensity	Final outcome	Onset date	Recovery date
A	Pre-treatment	METABOLISM AND NUTRITION DISORDERS	HYPOKALAEMIA	Moderate	Recovered	20-Oct-2008	27-Oct-2008
	On-treatment	GASTROINTESTINAL DISORDERS	FAECES HARD	Mild	Recovered	28-Oct-2008	31-Oct-2008
		GASTROINTESTINAL DISORDERS	FLATULENCE	Mild	Recovered	28-Oct-2008	07-Nov-2008
		SKIN AND SUBCUTANEOUS TISSUE DISORDERS	PRURITUS	Mild	Recovered	29-Oct-2008	24-Nov-2008
		INJURY, POISONING AND PROCEDURAL COMPLICATIONS	FALL	Moderate	Recovered	02-Nov-2008	02-Nov-2008
		INJURY, POISONING AND PROCEDURAL COMPLICATIONS	EXCORIATION	Mild	Recovered	02-Nov-2008	13-Nov-2008
		INVESTIGATIONS	CAROTID BRUIT	Mild	Unknown	07-Nov-2008	Unknown
	Post-treatment	NERVOUS SYSTEM DISORDERS	MENTAL IMPAIRMENT	Mild	Recovered	13-Nov-2008	03-Dec-2008
B	On-treatment	INJURY, POISONING AND PROCEDURAL COMPLICATIONS	FALL	Mild	Recovered With sequelae	22-Oct-2008	22-Oct-2008
		INJURY, POISONING AND PROCEDURAL COMPLICATIONS	JOINT SPRAIN	Moderate	Recovered With sequelae	22-Oct-2008	21-Nov-2008
		INJURY, POISONING AND PROCEDURAL COMPLICATIONS	CONTUSION	Mild	Recovered	22-Oct-2008	29-Oct-2008
		GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	FATIGUE	Moderate	Recovered	24-Oct-2008	29-Oct-2008
		PSYCHIATRIC DISORDERS	CONFUSIONAL STATE	Moderate	Recovered	29-Oct-2008	07-Nov-2008
	Post-treatment	GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	FATIGUE	Moderate	Not Recovered	12-Nov-2008	Unknown
		GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	IRRITABILITY	Moderate	Not Recovered	09-Dec-2008	Unknown
		NERVOUS SYSTEM DISORDERS	HEADACHE	Moderate	Not Recovered	09-Dec-2008	Unknown
		PSYCHIATRIC DISORDERS	CONFUSIONAL STATE	Moderate	Unknown	09-Dec-2008	Unknown

Conclusions: No conclusions regarding the original objectives of the study can be drawn due to the limited data collected in this study.

Date of report: 13-Feb-2009