Sponsor:	Istituto di Ricerche Farmacologiche Mario Negri – IRCCS Via G. La Masa 19, 20156 Milano
Study title:	"A pilot study to evaluate the incidence of hyponatremia in a medical-surgical hospital and to explore the efficacy and the safety of Tolvaptan in the clinical practice"
Short title:	Tolvaptan for In-Hospital Hyponatremia
Acronym:	INSERT
EudraCT:	2010-024431-17
Clinical Trial Registration:	NCT01386372
Phase:	II
Start date:	03/31/2011
LVLP:	07/26/2012 (prematurely halted before randomization)
Reason for interruption:	never started
Keywords:	Hyponatremia; vasopressin; Tolvaptan; SIADH

The study has been performed in compliance with Good Clinical Practice

Short Report

The study was organized in two phases. Phase one was an observational study aimed to evaluate the incidence and evolution of secondary hyponatremia in patients affected by frequent predisposing conditions such as heart failure, decompensated liver cirrhosis and nephrotic syndrome who were referred to a large general hospital. Phase two was an interventional randomized study aimed to assess the efficacy of Tolvaptan therapy for the treatment of secondary hyponatremia in this context. In the first phase we identified 268 patients over a screening period of nine months. This finding confirmed that hyponatremia is a very common problem in the reality of a large hospital. However, in all patients – with the exception of a very few of them with pre-terminal diseases - hyponatremia recovered fully within a few days, without tolvaptan. In three patients, sodium levels did not normalize despite correction of predisposing clinical conditions. Thus, 1.1% only of identified patients with hyponatremia had a potential indication to tolvaptan therapy. Thus, in everyday clinical practice awareness of the problem and appropriate correction of the predisposing factors are crucial for the treatment of hyponatremia. This consideration challenged the rationale for a clinical trial to test the efficacy of tolvaptan therapy in this context. Thus we closed the study for futility reasons without moving to phase two. At study closure no patient had been exposed to the experimental treatment.

In conclusion, our findings challenge the role of tolvaptan for the treatment of secondary hyponatremia in clinical practice. Avoiding unnecessary patient exposure to tolvaptan will prevent the risk of treatment-related side effects and will have relevant implications for health care providers because of the high costs of this medication.