A Multicenter Tolvaptan study For Uncontrolled volume overload in Japanese acute decompensated heart fallure patients: A prospective observational multicenter cohort study

MT FUJI study

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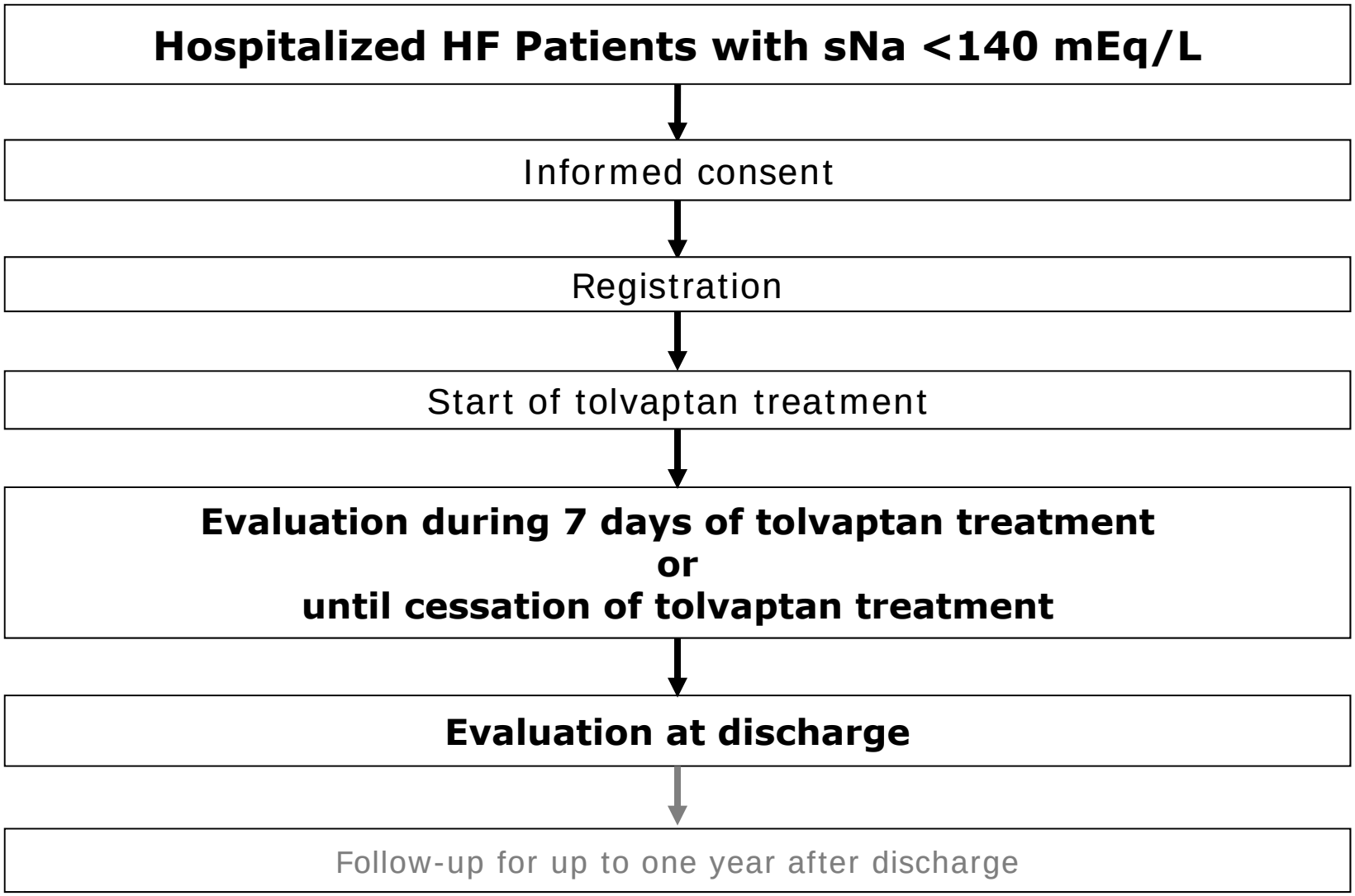
on behalf of the MT FUJI investigators

Goal

To clarify patient characteristics and outcome treated by tolvaptan in hypo-natremic HF patients, before a prospective randomized trial .

Outline of the study



Endpoints

- Efficacy and Safety -

1) Changes in signs and symptoms of congestion during treatment with tolvaptan

2) Changes in laboratory data (sNa, urinary volume, biomarkers, etc) during treatment with tolvaptan

3) Outcome

in-hospital mortality

one-year events after discharge

total death

Cardiovascular events

HF re-hospitalization, ventricular arrhythmia, ACS, Stroke

Cardiovascular death

HF, ACS, Stroke, sudden death, unknown, others

4) Exploratory analysis

efficacy and safety of tolvaptan treatment

outcome by tolvaptan treatment

Inclusion Criteria

Heart failure (HF) was diagnosed according to the Framingham criteria with BNP>100pg/ml or NT-proBNP>400 pg/ml.

1. Hospitalized for acute exacerbation of chronic HF presenting with congestion
2. Serum sodium level at admission < 140 mEq/L
3. Age >20 years old
4. Written informed consent signed before any study-specific procedure

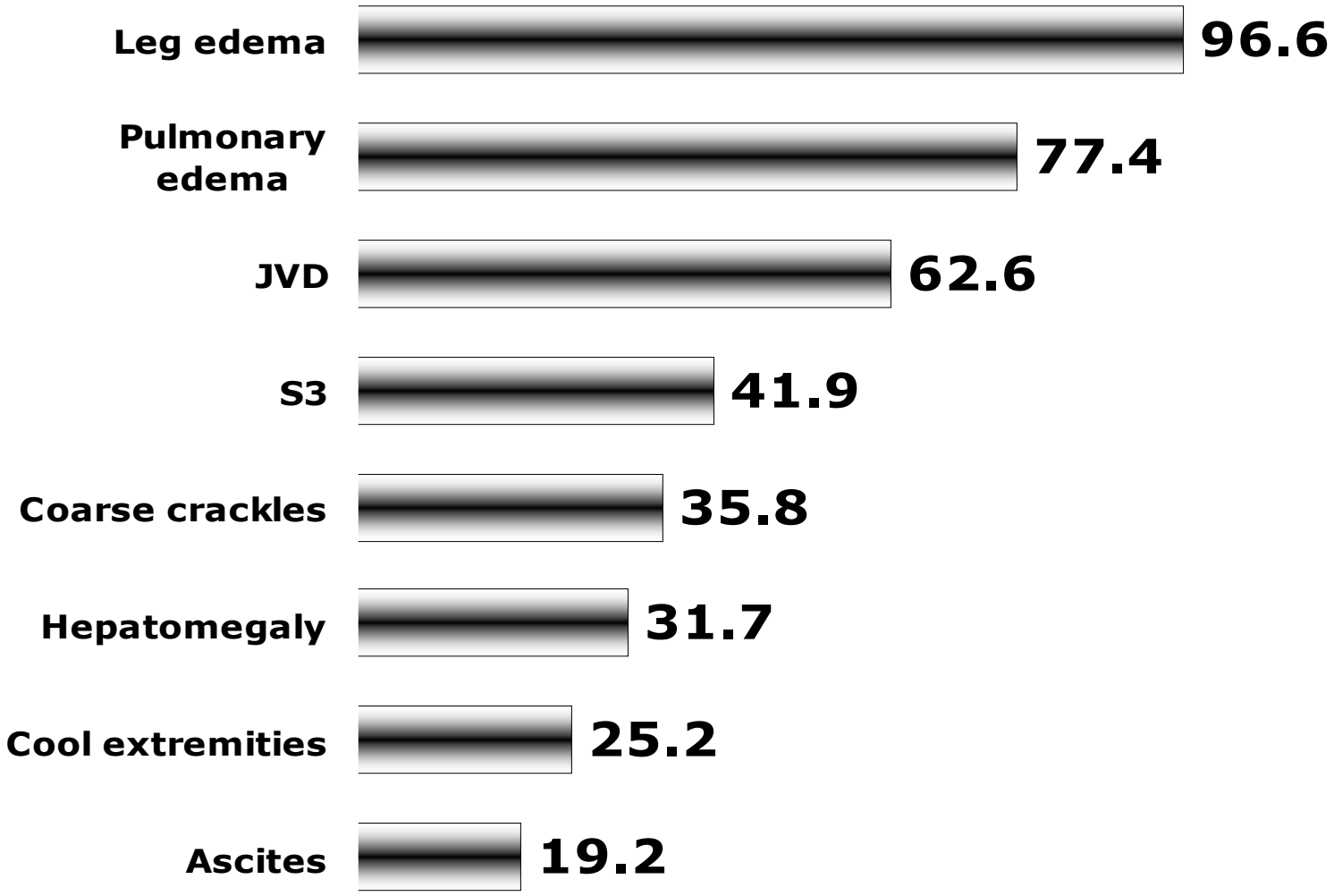
Exclusion Criteria

1. History of hypersensitivity to any component of this product or analogous compounds (mozavaptan hydrochloride, etc.)
2. Anuria
3. Lack of a sense of thirst or difficulty in taking water
4. Pregnant or possibly pregnant women
5. Under treatment with tolvaptan at the time of registration for this study
6. Diagnosed as having acute coronary syndrome or scheduled for coronary angioplasty during the study period
7. Judged by the physician-in-charge as being an unsuitable candidate for the study

Patient characteristics

Number of patients	**N**	**265**
Sex (n,%)	**Men**	**175,66**
	Women	**90,34**
Age (yrs)	**Mean**	**74.5±12.9**
Distribution of age (%)	**<50**	**5.7**
	50 - <65	**14.0**
	65 - <75	**23.4**
	75=<	**57.0**
Etiology (%)	**Ischemic**	**32.4**
	Hypertensive	**8.7**
	Cardiomyopathy	**20.4**
	Valvular	**27.2**
	others	**10.9**
	unknown	**0.4**
Prior hospitalization for HF (%)	**Yes**	**35.1**
	No	**63.8**
	unknown	**1.1**

Signs and symptoms before TLV



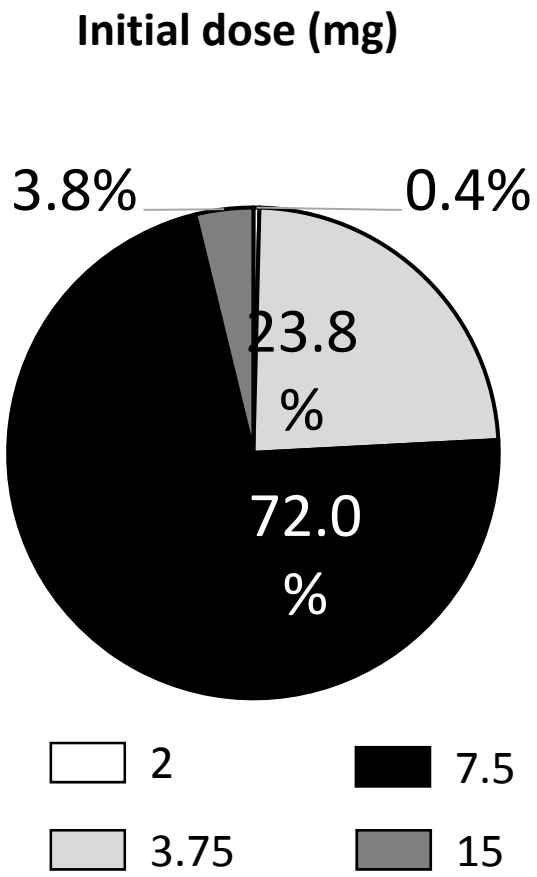
Data are shown in percentage. TLV, tolvaptan; JVD, jugular venous distension; S3, third heart sound.

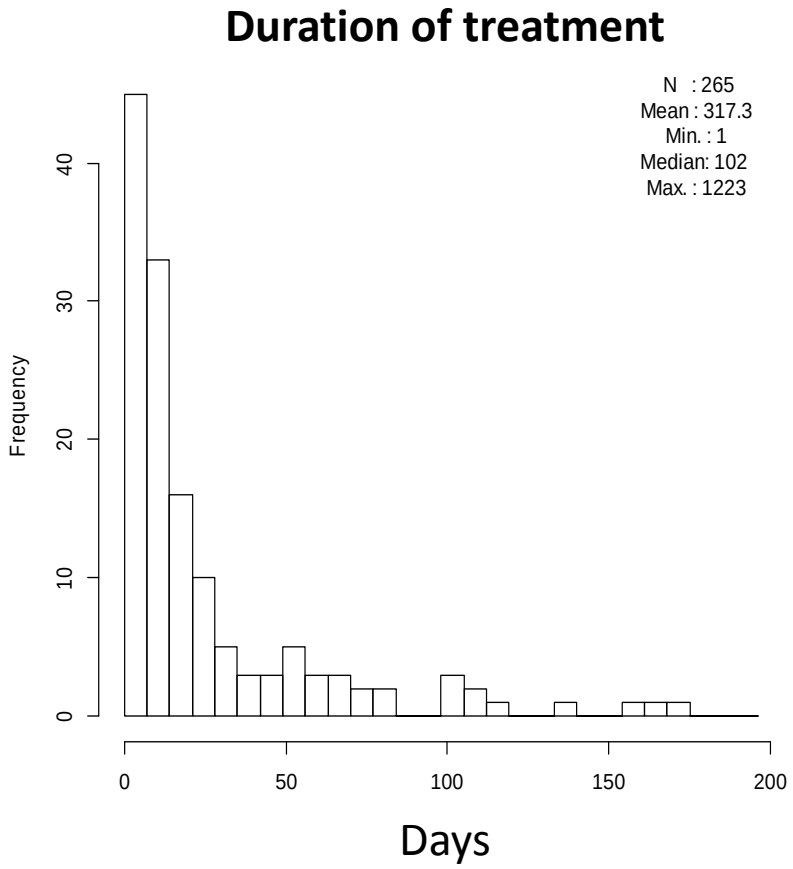
Baseline data (1)

	Mean	SD
SBP [mmHg]	110.8	22.0
DBP [mmHg]	61.2	12.5
HR [bpm]	76.0	17.2
Alb [g/dL]	3.41	0.60
Cre [mg/dL]	1.45	0.80
Na [mEq/L]	134.8	4.5
K [mEq/L]	4.19	0.55
Cl [mEq/L]	99.4	6.2
BUN [mg/dL]	30.8	16.4
sOsm [mOsm/L]	298.9	158.8
T-Bil [mg/dL]	1.11	0.82
eGFR [mL/min/1.73m^2]	43.7	21.5
uOsm [mOsm/L]	398.2	134.3

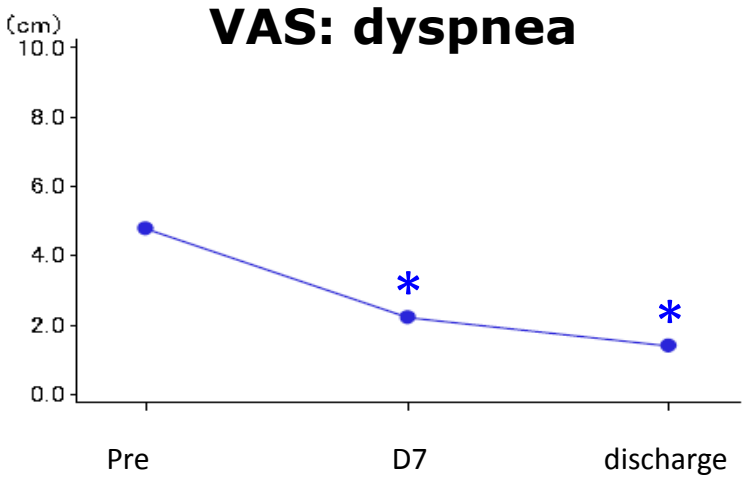
SBP, systolic blood pressure; DBP, diastolic BP; HR, heart rate; Alb, serum albumin; Cre, serum creatinine; BUN, blood urea nitrogen; sOsm, serum osmolality; uOsm, urinary Osm.

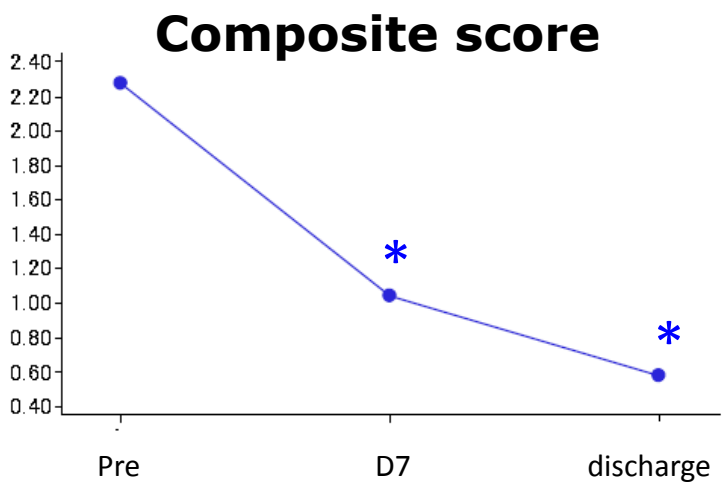
Dose and duration of Tolvaptan

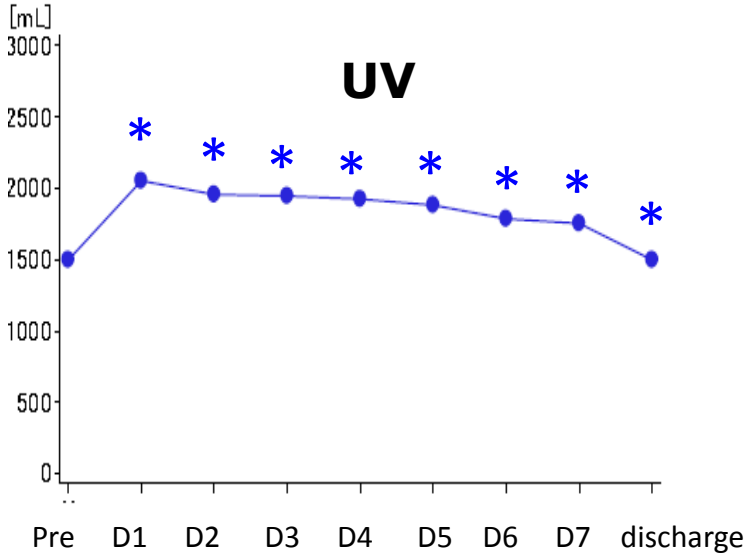


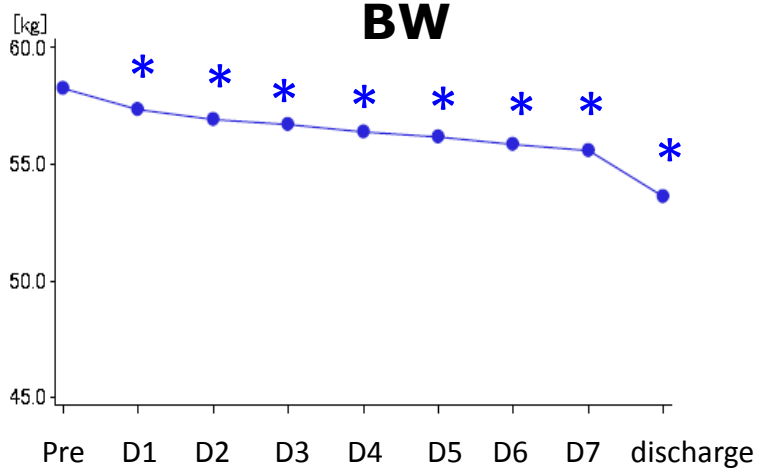


Changes in congestion



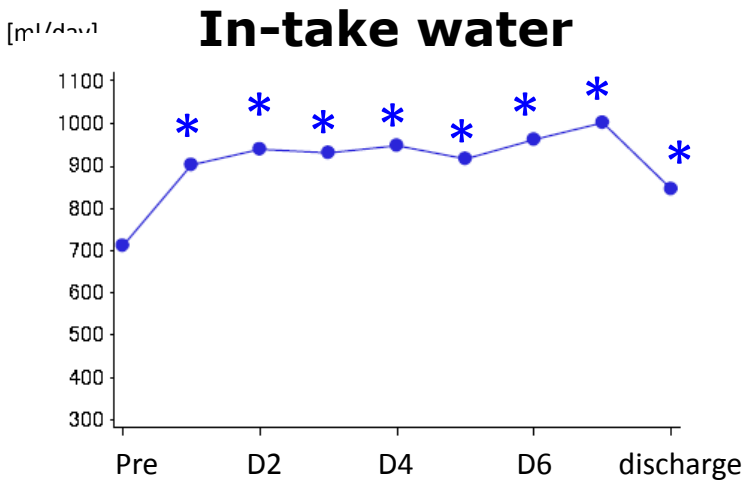


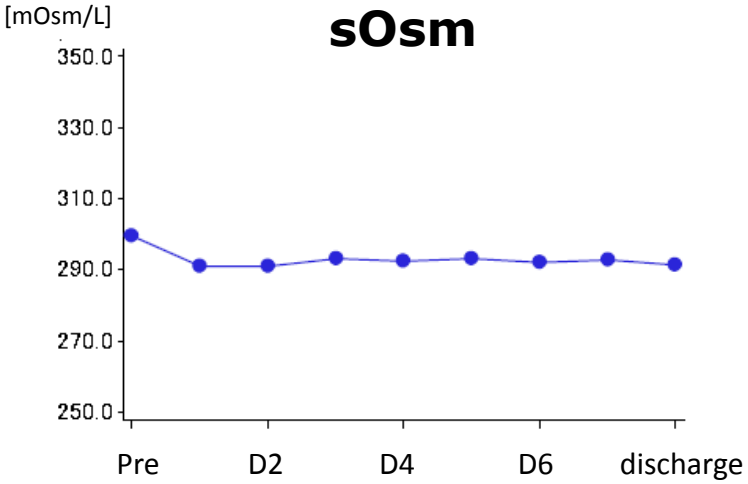


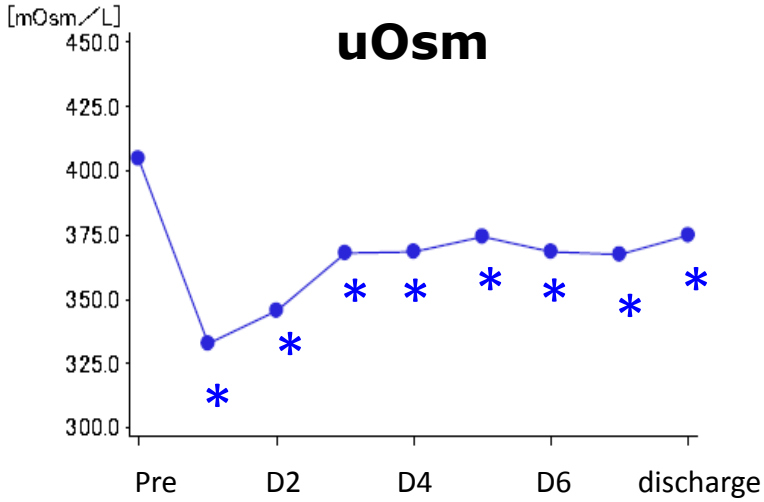


The figure was shown the LSMeans by visit calculated by MMRM method and the statistical tests with baseline used Holm's multiple comparison adjustment.
*: $p<0.05$ between baseline

Changes in parameters (1)







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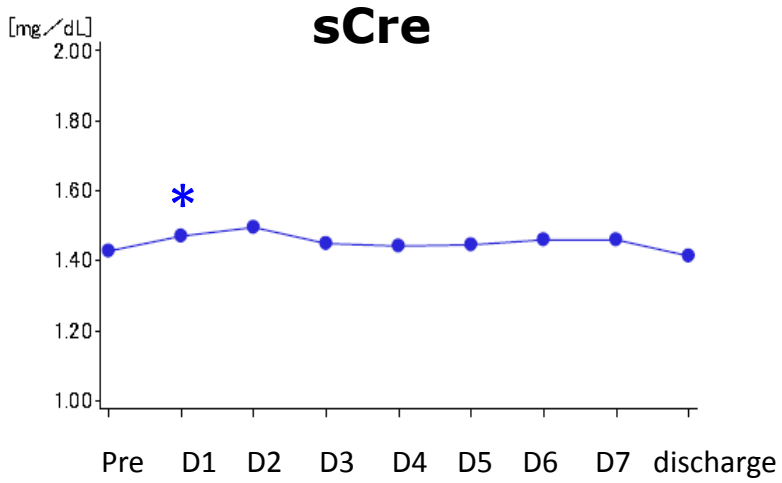
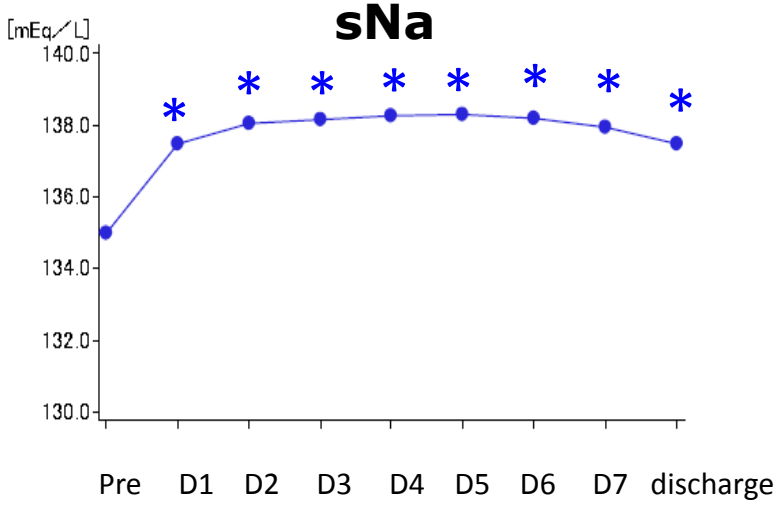
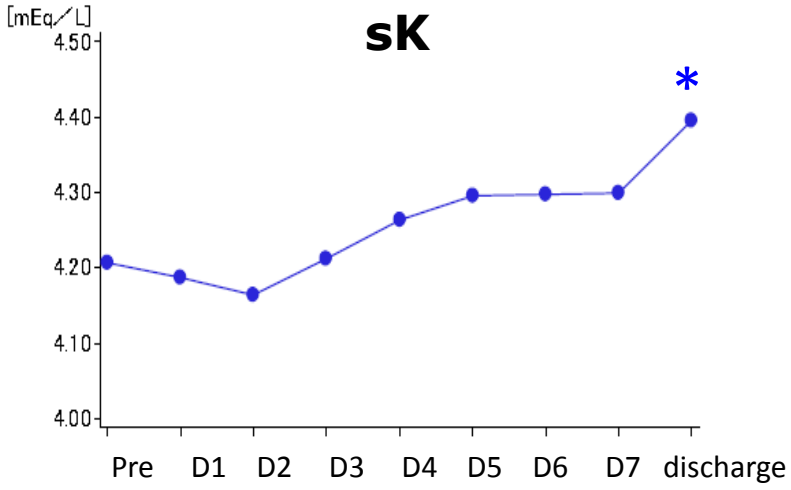
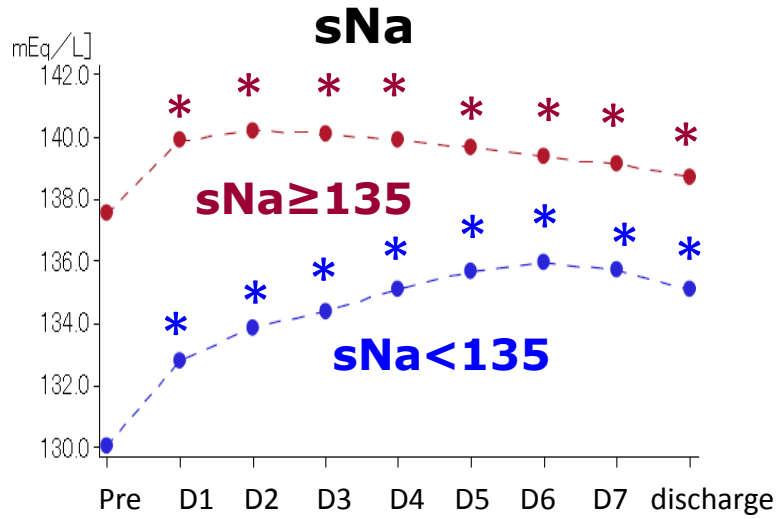
Changes in parameters (2)









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Summary & conclusion

The present study confirmed that beneficial effects of tolvaptan even in hyponatremic HF patients.

Based on these results of the present study, further analysis should be performed. Then, further prospective study to clarify improved outcome by tolvaptan should be conducted in such high risk populations.

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