# TRANSFORM HF

## *TORSEMIDE VS FUROSEMIDE*

*Κουτρουλός Μάριος-Βασίλειος*
*Ειδικευόμενος Καρδιολογίας*
*Πανεπιστημιακή Καρδιολογική Κλινική*
*Π.Γ.Ν.Αλεξανδρούπολης*
*Διευθυντής: καθ. Τζιακάς Δημήτριος*

# BACKGROUND

- Loop Diuretics are routinely used to manage congestion in patients with heart failure
- Furosemide: most commonly used
- Torsemide: may offer advantages over furosemide

# Intervention Model

- *parallel assignment*

- *randomized, unblinded, two-arm, multi-center clinical trial of patients with heart failure who are hospitalized*

# INCLUSION CRITERIA

- Patient hospitalized (≥ 24 hours or over a change in calendar date) with worsening of chronic heart failure, or new diagnosis of heart failure AND meets one of the following criteria:
  - Has a left ventricular ejection fraction (EF) ≤40% within 24 months prior to and including index hospitalization by any method (with most recent value used to determine eligibility)
  - Has an elevated natriuretic peptide level (either NT-pro-B-type natriuretic peptide or B-type natriuretic peptide) during index hospitalization as measured by local laboratory (with most recent value used to determine eligibility)
- Plan for a daily outpatient oral loop diuretic regimen upon hospital discharge with anticipated need for long-term loop diuretic use
- ≥ 18 years of age
- Signed informed consent

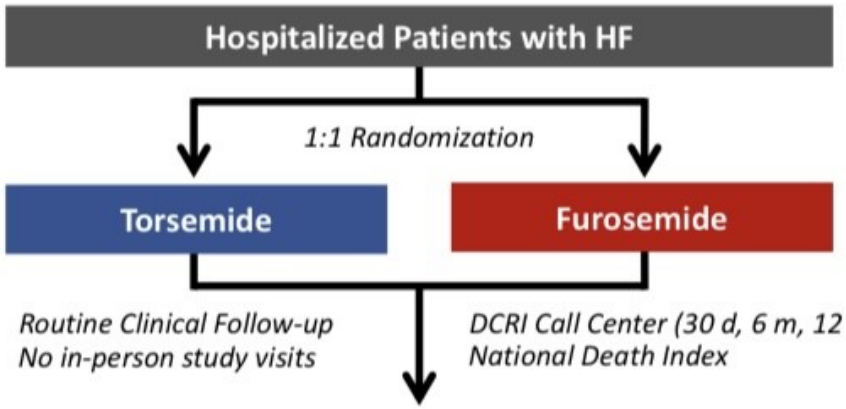
# EXCLUSION CRITERIA

- End-stage renal disease requiring renal replacement therapy
- Inability or unwillingness to comply with the study requirements
- History of heart transplant or actively listed for heart transplant
- Implanted left ventricular assist device or implant anticipated <3 months
- Pregnant or nursing women
- Malignancy or other non-cardiac condition limiting life expectancy to <12 months
- Known hypersensitivity to furosemide, torsemide, or related agents

# Design

**Primary Objective:** Compare the **treatment strategy** of torsemide vs. furosemide on long-term clinical outcomes among patients hospitalized with HF through a pragmatic trial

TRANSFORM-HF




**Regardless of EF**
**Long-term plan for loop diuretic**
**(60 US Sites)**

**Open-Label**
Dosing per Clinician

**Primary Hypothesis:**
Torsemide reduces mortality by 20% vs. furosemide

**Primary Endpoint:**

**All-Cause Mortality**

**Event-Driven**
721 Death Events
(85% power)

**Secondary Endpoints:**

**All-cause Mortality + All-cause Hospitalization**
**Total Hospitalizations**
Health-related Quality of Life (KCCQ)
Symptoms of Depression (PHQ-2)

Greene SJ, Mentz RJ, et al. JACC Heart Fail 2021; 9(5):325-335.

ClinicalTrials.gov Identifier: NCT03296813

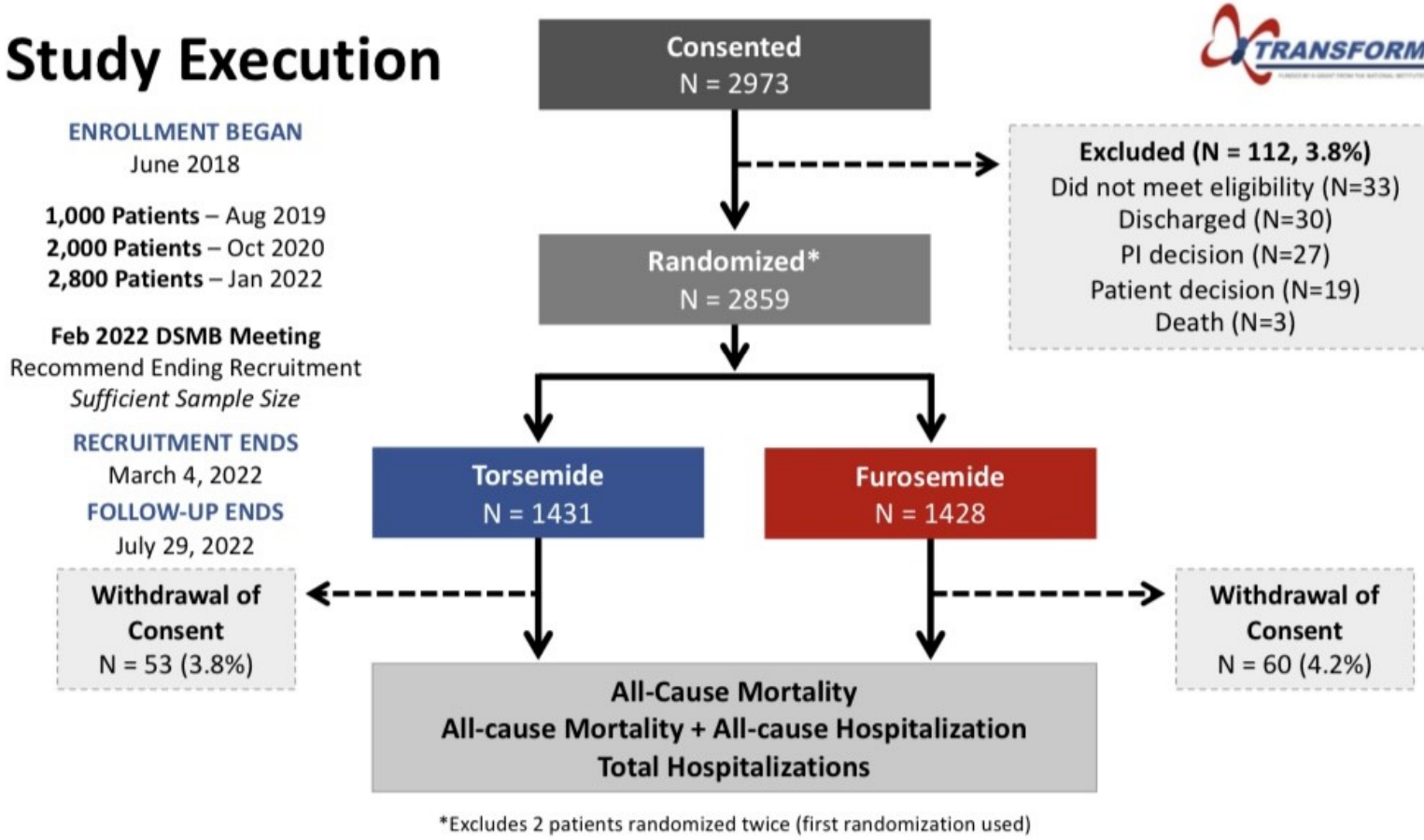
# Study Execution

**ENROLLMENT BEGAN**
June 2018

**1,000 Patients** – Aug 2019
**2,000 Patients** – Oct 2020
**2,800 Patients** – Jan 2022

**Feb 2022 DSMB Meeting**
Recommend Ending Recruitment
*Sufficient Sample Size*

**RECRUITMENT ENDS**
March 4, 2022
**FOLLOW-UP ENDS**
July 29, 2022




*Excludes 2 patients randomized twice (first randomization used)

# Baseline Characteristics

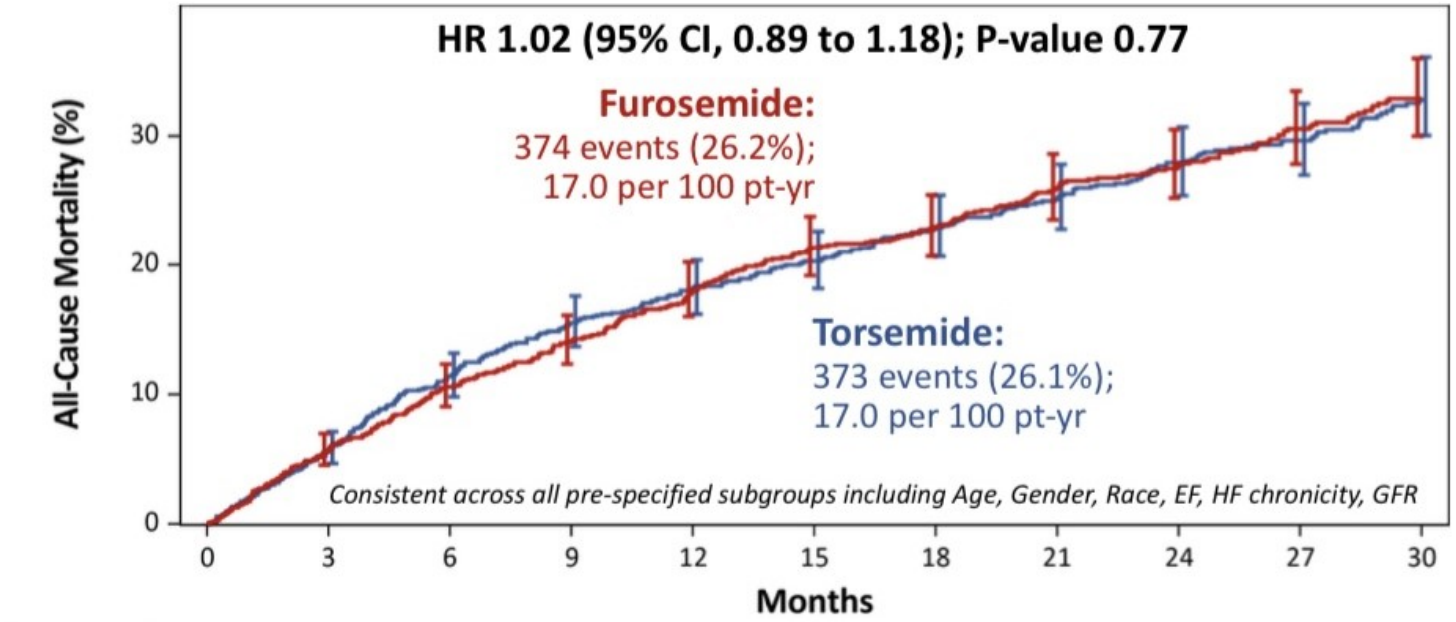
| Characteristics | Torsemide (N=1431) | Furosemide (N=1428) |
|---|---|---|
| Age (yr) | 64±14 | 65±14 |
| Women | 35% | 39% |
| White race | 58% | 59% |
| Black race | 33% | 35% |
| Newly diagnosed HF | 30% | 29% |
| EF ≥50% | 22% | 23% |
| 41-49% | 6% | 5% |
| ≤40% | 65% | 63% |
| NT-proBNP (pg/mL) | 3994 (1938, 8850) | 3833 (1936, 7807) |
| Ischemic etiology | 30% | 27% |
| Systolic blood pressure (mmHg) | 118±19 | 119±21 |
| Body mass index (kg/m$^2$) | 32±10 | 32±9 |
| eGFR (ml/min/1.73 m$^2$) | 59±25 | 60±26 |

Presented as %, Mean ± SD or median (IQR)

**LVEF≤40% (N=1836)**

| HFrEF Therapy | |
|---|---|
| Beta-blocker | 82% |
| ACE/ARB/(ARNI) | 68% (25%) |
| MRA | 44% |
| SGLT2i | 8% |

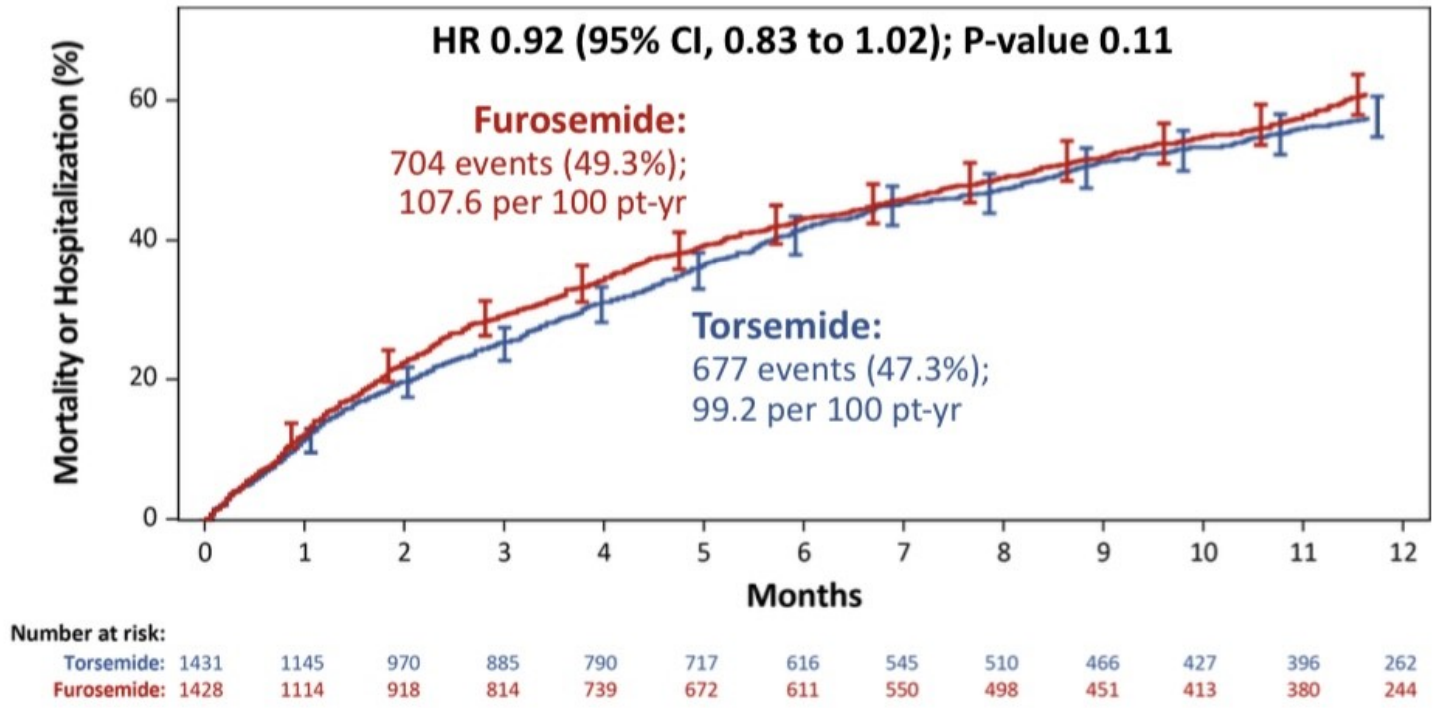
# Primary Endpoint: All-Cause Mortality




| Number at risk: | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Torsemide: | 1431 | 1301 | 1135 | 1027 | 904 | 787 | 689 | 661 | 543 | 434 | 317 |
| Furosemide: | 1428 | 1295 | 1151 | 1036 | 897 | 782 | 707 | 658 | 542 | 428 | 317 |

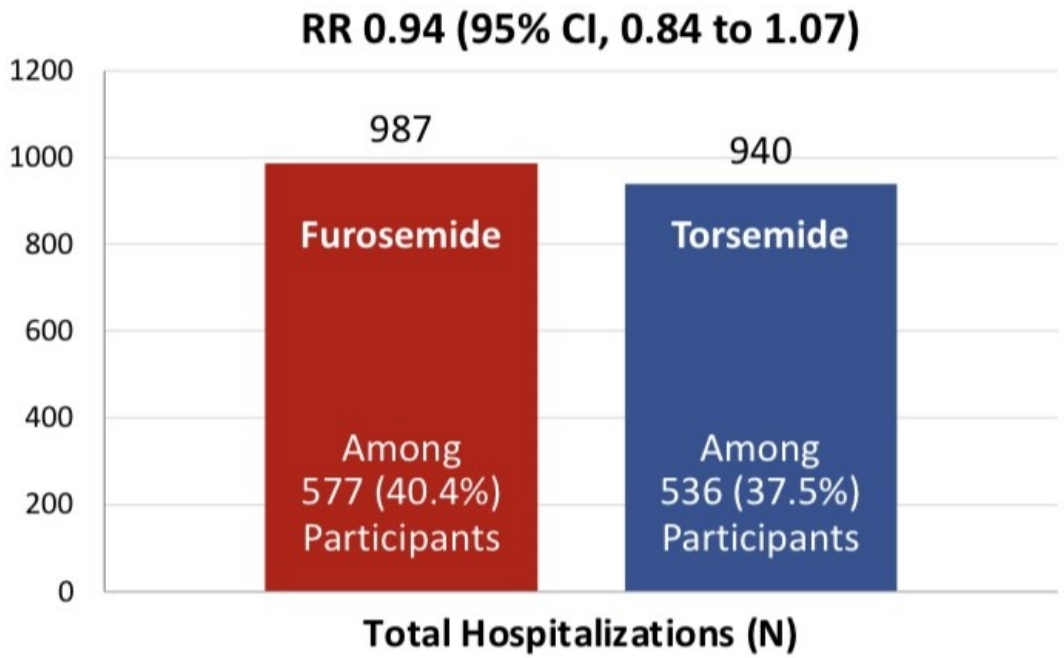
Median follow-up: 17.4 months (IQR: 8.0 to 29.0)

# All-Cause Mortality or Hospitalization (12 mos)

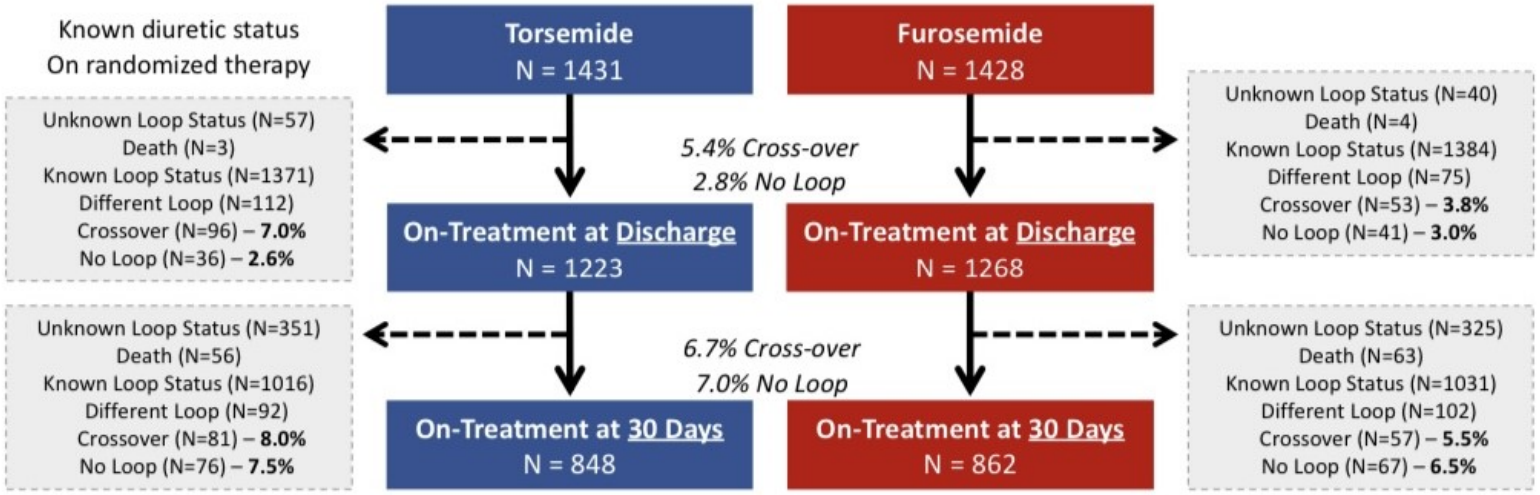



| Number at risk: | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Torsemide: | 1431 | 1145 | 970 | 885 | 790 | 717 | 616 | 545 | 510 | 466 | 427 | 396 | 262 |
| Furosemide: | 1428 | 1114 | 918 | 814 | 739 | 672 | 611 | 550 | 498 | 451 | 413 | 380 | 244 |

# Total Hospitalizations (12 mos)



# On-Treatment Analysis (Pre-Specified)




| | ITT Analysis | On-Treatment at Discharge | On-Treatment at 30 Days |
|---|---|---|---|
| All-cause mortality | **1.02 (0.89, 1.18)** P=0.76 | **0.99 (0.85, 1.15)** P=0.86 | **0.96 (0.78, 1.18)** P=0.69 |
| All-cause mortality or all-cause hospitalization | **0.92 (0.83, 1.02)** P=0.11 | **0.91 (0.81, 1.01)** P=0.082 | **0.89 (0.78, 1.02)** P=0.10 |

# LIMITATIONS

- Cross-overs and diuretic discontinuation would bias toward neutral results
- Dose was left to clinician discretion which may have influenced results
- All-cause outcomes may have been too imprecise for measuring differences especially during the COVID-19 pandemic
- No assessment of other adverse events (e.g., worsening renal function, electrolyte abnormalities or non-hospitalization events)

# CONCLUSION

- • A strategy of torsemide had similar effectiveness compared with a strategy of furosemide for the clinical outcomes of mortality and hospitalization in patients hospitalized with heart failure.
- Clinical time should be spent focusing on appropriate diuretic dosing and prioritizing guideline-directed medical therapy (GDMT) initiation / titration

# THANK YOU

When you check your watch
to see if it's time to
take your furosemide