Non-participation in a heart failure clinical trial: perspectives and opportunities from the VICTORIA trial and simultaneous registry

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Background

- Randomized controlled trials (RCT) often enroll patients with differing demographics and outcomes as compared to a broader non-RCT population.
- To provide context for the VerICiguaT Global Study in Subjects With Heart Failure With Reduced Ejection Fraction (VICTORIA) trial, we designed a contemporaneous registry of patients with worsening heart failure (WHF) to characterize baseline characteristics, outcomes and potential reasons for non-participation in a RCT.

Methods

- The VICTORIA Registry enrolled patients hospitalized for HF with reduced ejection fraction (HFrEF) at 51 sites across the United States and Canada.
- Eligible patients for the registry included those with chronic HF, currently or recently hospitalized for HF, and an ejection fraction <45%; no other exclusions were applied.
- Sites were asked to identify 50 patients for retrospective chart data abstraction sampled over 4 different time points between February 2018 and January 2019 during the RCT enrollment period.
- VICTORIA RCT trial eligibility criteria were applied and non-mutually exclusive reasons for non-inclusion were captured where available.
- Patients are classified as Not Eligible (1256 patients), Eligible and not Enrolled (766 patients) and Enrolled into RCT (34 patients; data not shown).
- 1-year outcomes were estimated by the MAGGIC score for patients in the Registry and actual outcomes for the RCT.

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Results

Table 1. Baseline Patient Characteristics.

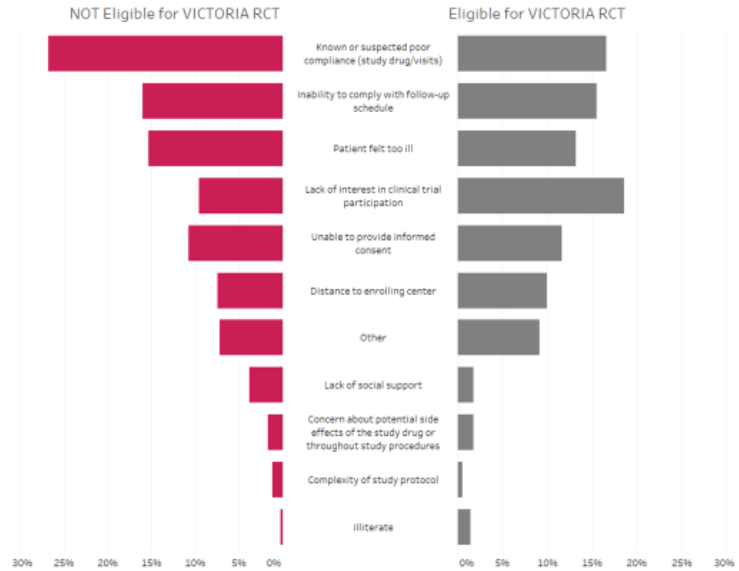
	Registry		RCT
Characteristic	Not eligible N=1256	Eligible, Not Enrolled N=766	North American patients N=560
Age, years	70 (59-80)	72 (61-82)	68 (58-75)
Women, %	33.1	34.7	26.8
White Race, %	62.2	59.0	76.4
Medical History/Tests (%)			
CAD	58.2	60.6	63.0
Diabetes	49.9	45.4	56.7
Atrial fibrillation	46.5	49	47.9
Ejection fraction	25 (20-35)	25 (20-35)	26 (20-35)
ECG with atrial arrhythmia	20.9	26.4	18.4
Vital signs at discharge			
Systolic BP (mmHg)	114 (101-129)	115 (103-129)	117 (107-127)
Heart rate (bpm)	76 (67-86)	76 (68-85)	71 (64-81)
Labs at discharge			
eGFR (ml/min/1.73m^2)	51 (33-60)	51 (36-61)	55 (40-75)
NT-proBNP (discharge, pg/ml)	3640 (1506, 7760)	6581 (3057, 16060)	2412 (1285-4735)
MAGGIC Risk Score	28 (23-32)	28 (23-32)	24 (20-29)
1-year mortality rate, %	20.9 (estimated)	20.9 (estimated)	21.2 (actual)

Data represent median (25-75%ile) or %

Table 2. Select reasons for Non-Eligibility for VICTORIA RCT

Select Patient Exclusion Reasons for Non-Enrollment of Key Interest or > 10% Prevalence (Non-mutually exclusive)	Not Eligible for RCT (N=1256), %
Did not meet natriuretic peptide cutoff	8.5
No recent LVEF (assessed > 12 months prior to randomization)	0.9
Most recent LVEF >= 45%	0.7
Receipt of intravenous treatment < 24 hours prior to when randomization was considered	2.9
SBP <100 mmHg or symptomatic hypotension	12.0
Concurrent or anticipated use of long acting nitrates or NO donors	22.5
Is awaiting heart transplantation, receiving IV inotrope infusion, or anticipated need for VAD	8.0
Primary valvular heart disease requiring intervention or < 3 months after valvular intervention	5.3
Has tachycardia-induced cardiomyopathy and/or uncontrolled tachyarrhythmia	3.2
Acute coronary syndrome or coronary revascularization within 60 days	5.7
eGFR < 15 ml/min/1.73m^2 or receiving chronic dialysis therapy	8.5
Hepatic insufficiency such as cirrhosis or hepatic encephalopathy	2.2
Malignancy or non-cardiac condition limiting life expectancy < 3 years	5.7
Requires continuous home oxygen for severe pulmonary disease	9.2
Current alcohol and/or drug abuse	10.7
Other	16.7

Figure 1. Patient-specific Reasons for RCT Non-participation



Conclusions

- Patients with WHF enrolled in a contemporaneous registry exhibit high-risk features with many having modifiable reasons for exclusion from an RCT.
- Several reasons for non-participation in an RCT indicate opportunities for improving enrollment to ensure generalizability.

DISCLOSURES

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