UT Southwestern Medical Center

Parkland

Scientific Sessions

POLYPILL FOR HEART FAILURE WITH REDUCED EJECTION FRACTION: THE POLY-HF TRIAL

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PRESENTER DISCLOSURES

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Ambarish Pandey reports Research support: American Heart Association, Anumana, AstraZeneca, National Institute of Health, Roche Diagnostics, SC Pharmaceuticals, SQ Innovation, and Ultromics

- **Consultant:** Northwestern University, Tricog Health Inc, Lilly USA, Rivus, Cytokinetics, Roche Diagnostics, Sarfez Therapeutics, Edwards Lifesciences, Merck, Bayer, Anumana, Novo Nordisk, Alleviant, Pfizer, Abbott, iRhythm, Axon Therapies, Kilele Health, Acorai, Ultromics, Kardigan, Novartis, Idorsia Pharma, and Science37
- **Non-financial support:** Dr. Pandey is also a consultant for Palomarin, Inc. with stocks compensation

Thomas Wang reports the following:

- Co-inventor on a provisional patent application related to machine technology for producing combination pills.

BACKGROUND

- Heart failure (HF) is associated with high burden of morbidity and mortality
- Quadruple GDMT reduces mortality by ~50%, but only 15% of patients receive it
- **Barriers:** Provider inertia, pill burden, poor adherence
- **Polypill approach:** Multiple medications in a single pill; proven in ASCVD prevention
- GDMT regimen are complex and may not be well suited for a one-pill for all approach

STUDY OBJECTIVES

To evaluate the effects of a polypill-based approach vs. enhanced usual care on:

- LVEF at 6 months (primary)
- Clinical outcomes, quality of life, functional capacity, NT-proBNP, and adherence
- GDMT utilization and safety

STUDY DESIGN

Open-label RCT, two centers in Dallas, TX (Nov 2021-Oct 2025)

Adults with HFrEF (EF ≤40%)
not on target dose GDMT

Polypill
vs.
Enhanced usual care

Primary Endpoint:
LVEF at 6 months by CMR

STUDY INTERVENTION

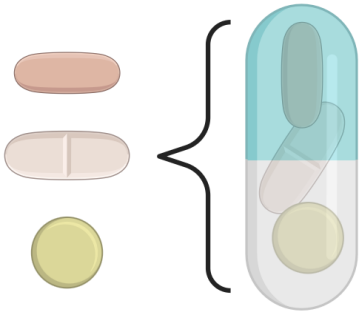
1:1 randomization to:

Over-Encapsulation Polypill

Metoprolol Succinate
(25/50/100/150 mg)

Empagliflozin
10 mg

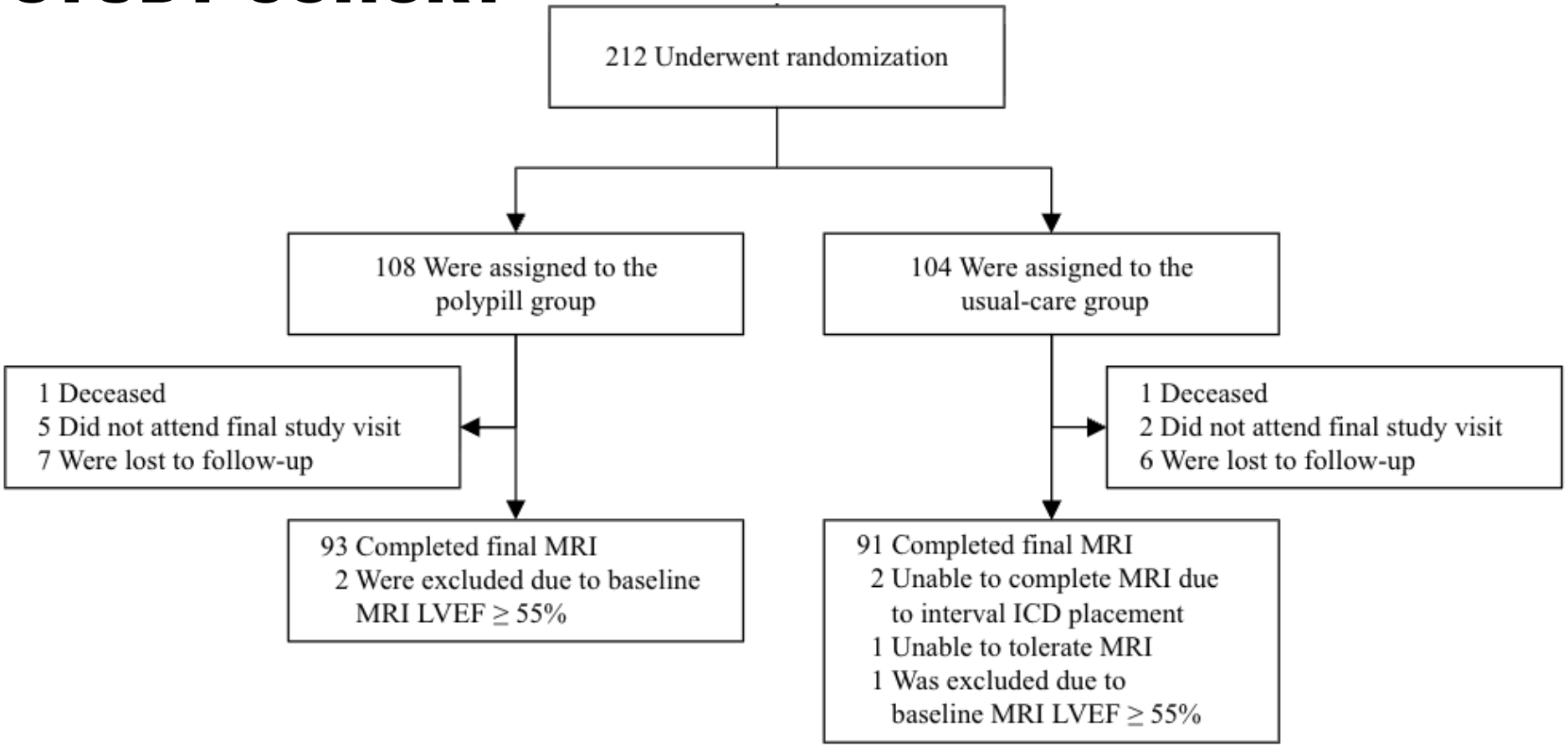
Spironolactone
12.5 mg



Vs.

Enhanced Usual Care

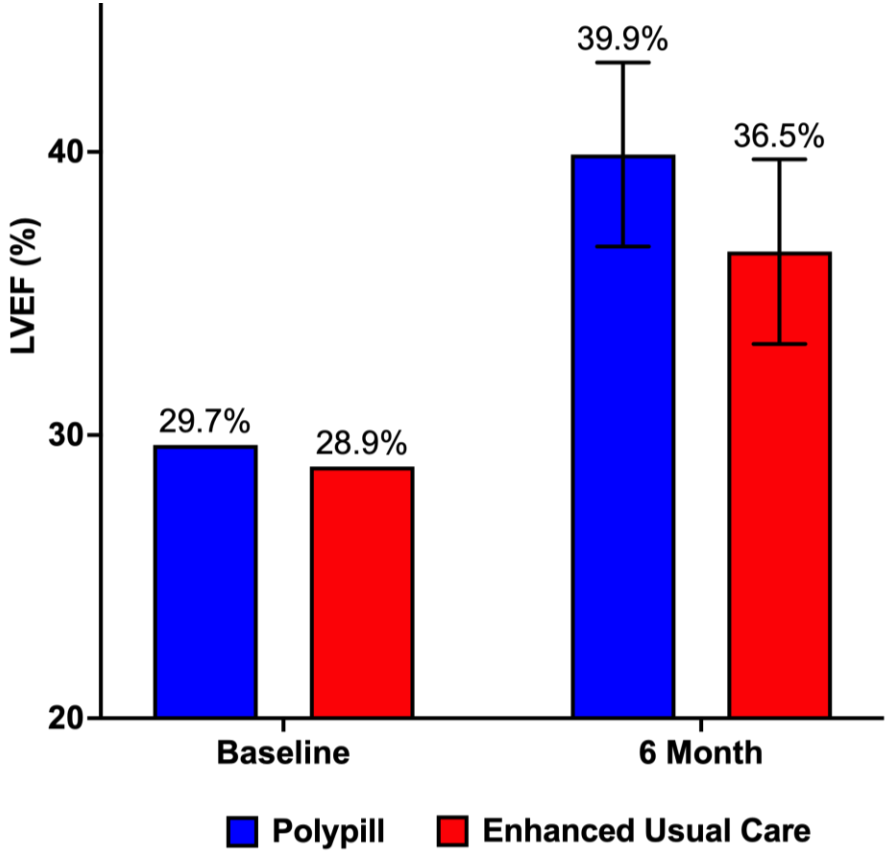
STUDY COHORT



BASELINE CHARACTERISTICS

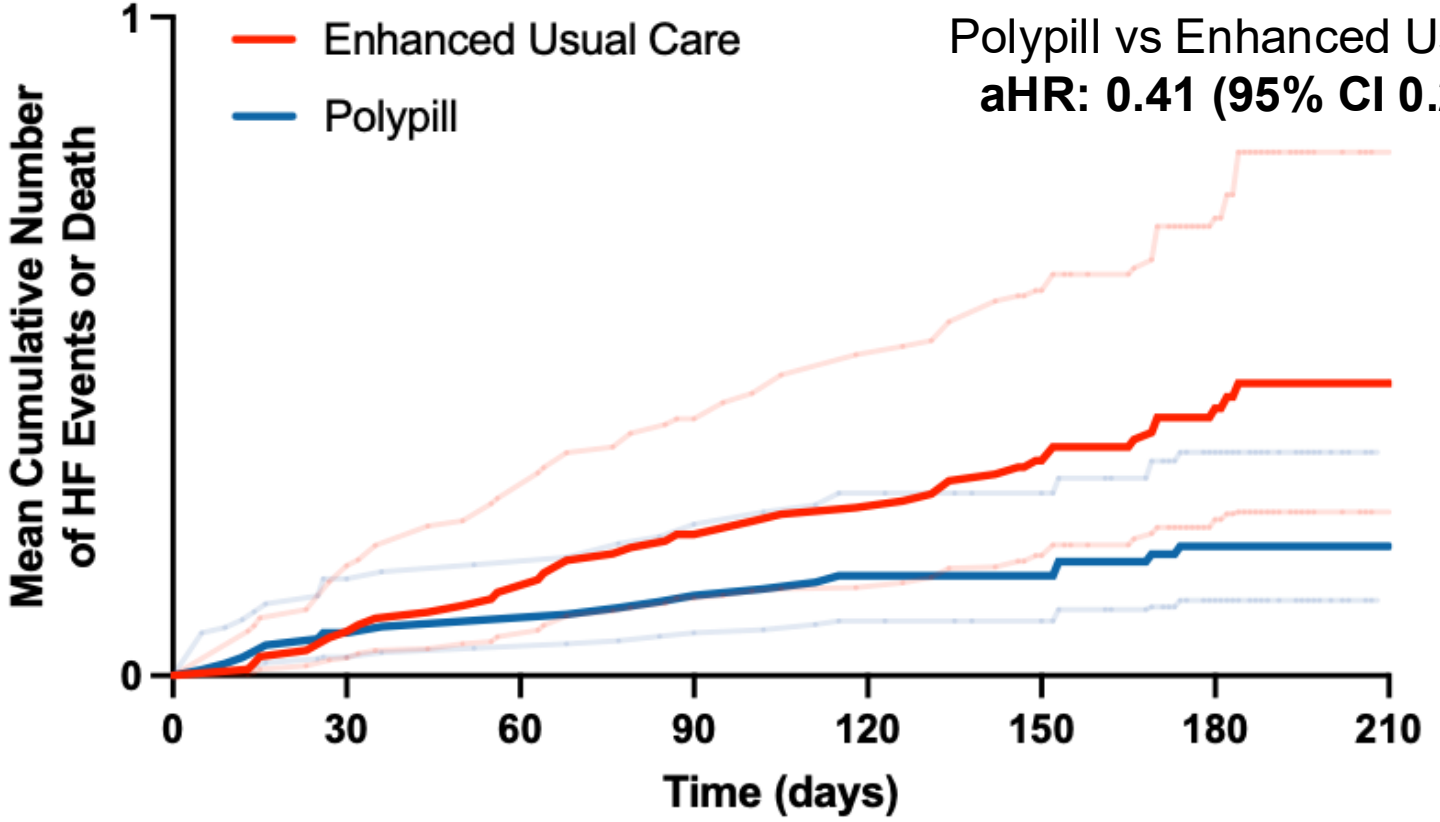
Characteristic	Polypill (N=108)	Enhanced Usual Care (N=104)
Age, years	53.5	53.5
Female sex, %	22	22
Black race, %	55	53
Hispanic ethnicity, %	32	35
Uninsured or county-sponsored coverage, %	69	66
LVEF by CMR, %	26	26
NT-proBNP, pg/mL	965	957
New-onset HF	52	54
GDMT Utilization at Baseline		
Beta-blockers, %	86	90
ACEi/ARB/ARNi, %	94	92
MRA, %	73	78
SGLT2i, %	65	68
Quadruple GDMT at any dose, %	**44**	**52**
Values shown are % or median		

PRIMARY OUTCOME – LVEF AT 6 MONTHS BY CMR



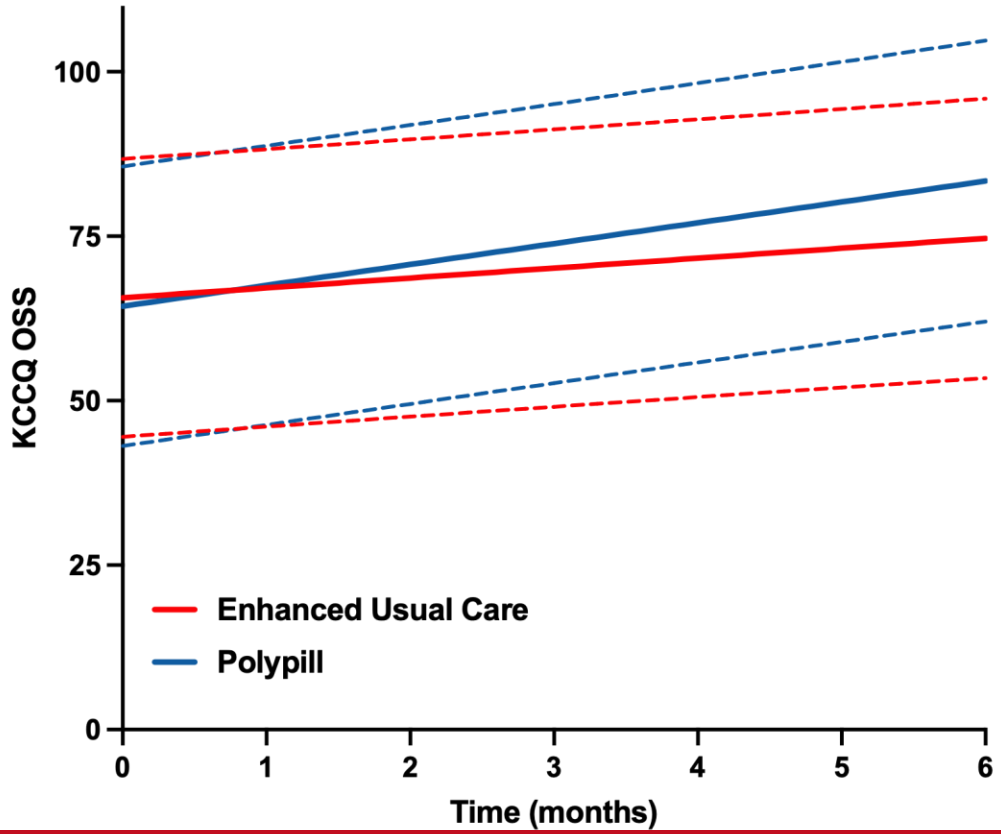
- Between-group difference: **3.4% (95% CI 0.46, 6.40), P = 0.02**
- Similar findings were observed in LVEF by echocardiogram at 6 months.
- Consistent treatment effects were noted across subgroups

CUMULATIVE HF EVENTS OR DEATH



Polypill vs Enhanced Usual Care:
aHR: 0.41 (95% CI 0.24, 0.71)

QUALITY OF LIFE BY KCCQ-OSS



6-Month

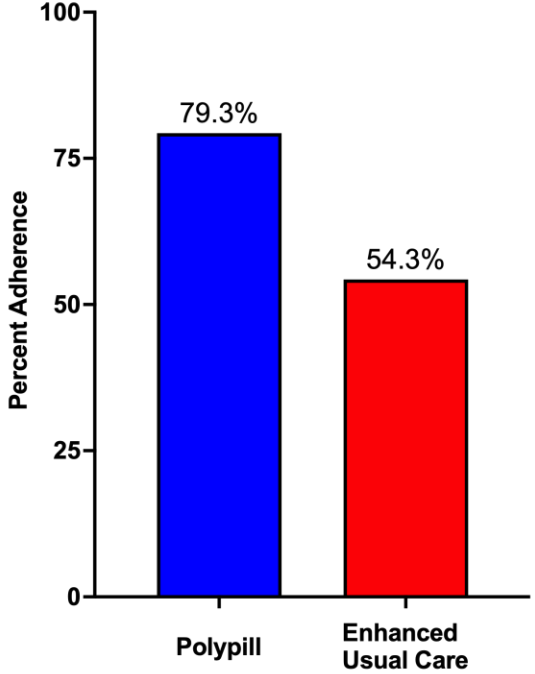
Polypill: 71.8

Enhanced Usual Care: 63.3

8.5(95% CI 2.6, 14.4)
P = 0.005

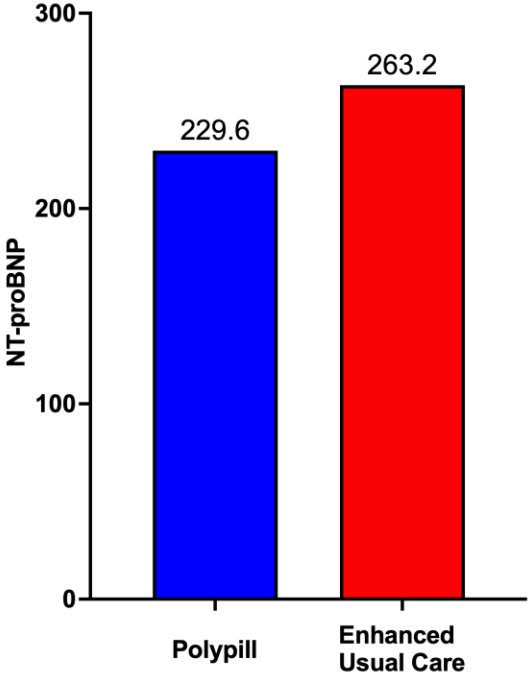
Adherence

Adherent vs Non-adherent
RR: 1.50 (1.05, 2.16), p<0.03



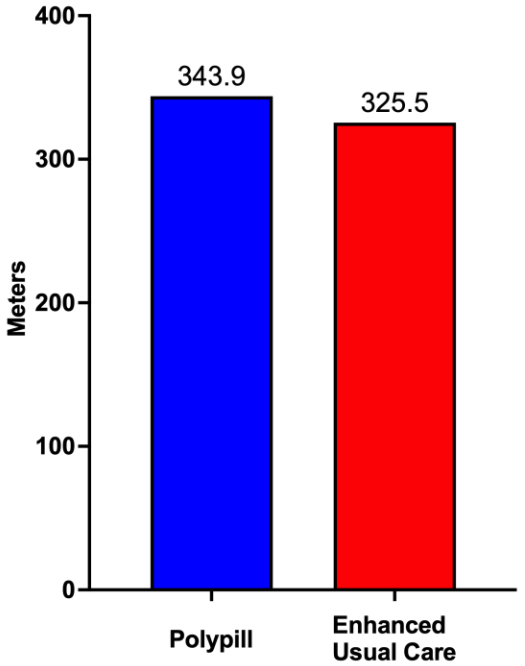
NT-ProBNP

Geometric Mean Ratio:
0.87 (0.65, 1.18), p=0.37

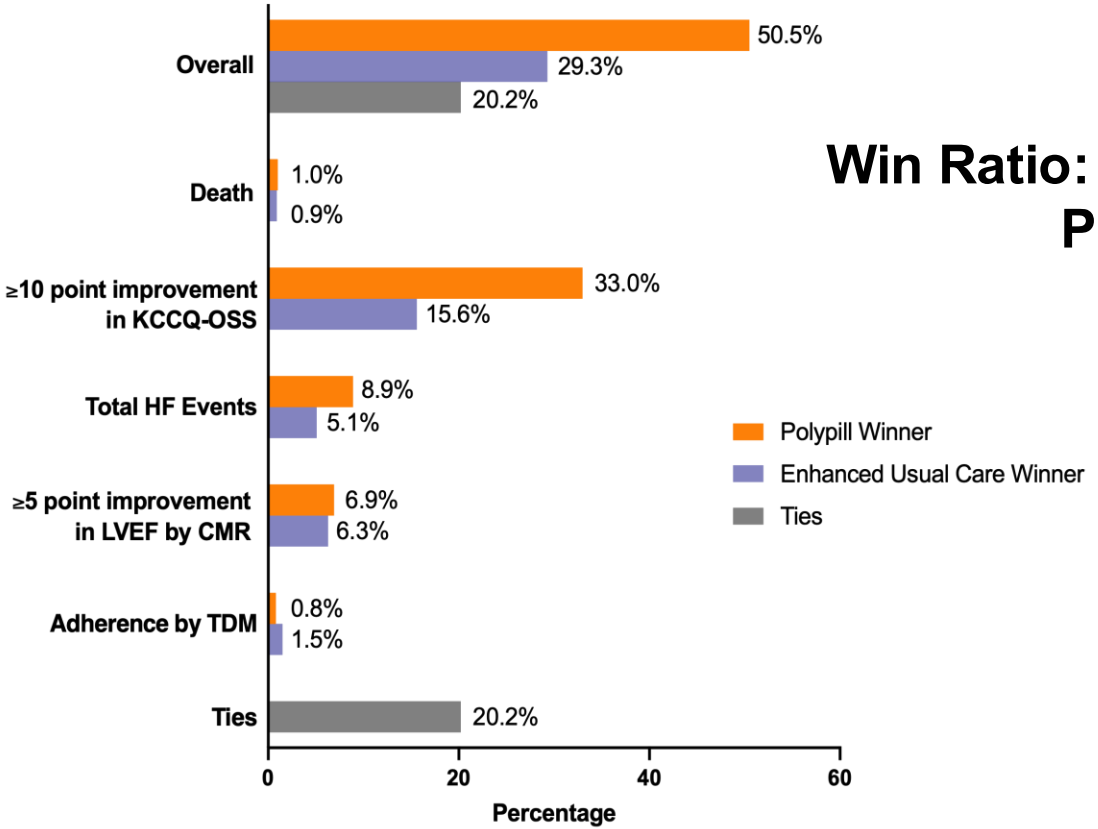


6MWD

Difference
18 m (-6, 43), p = 0.15

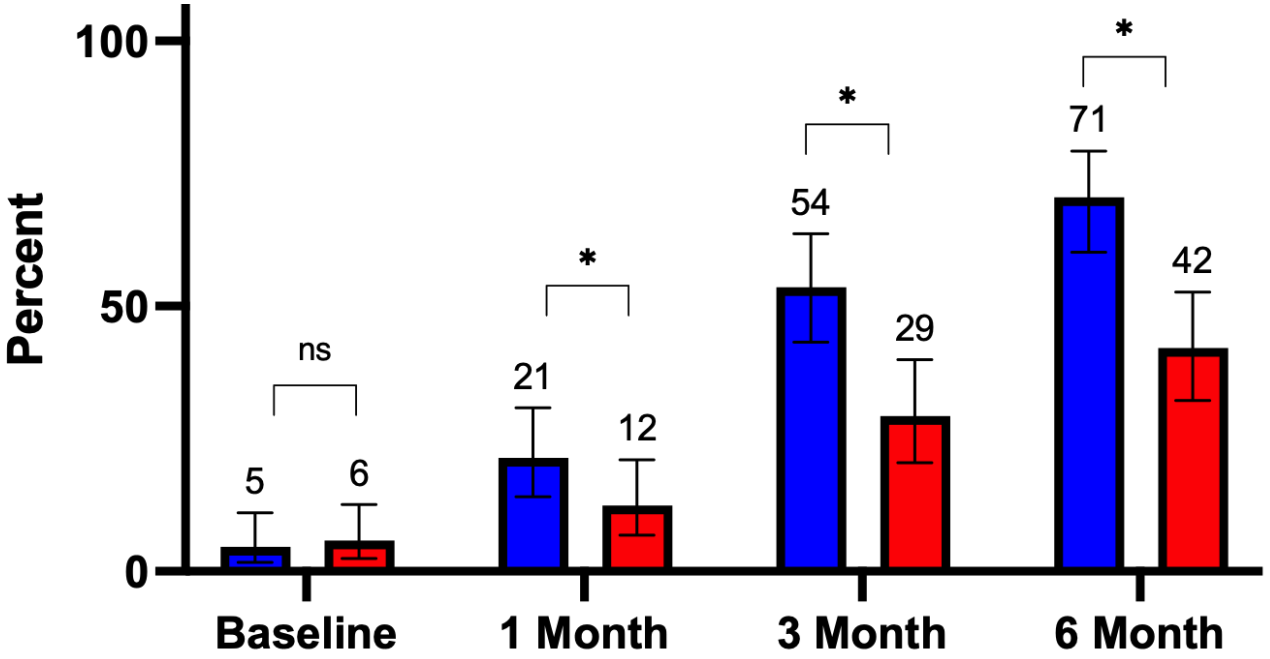


WIN RATIO HIERARCHICAL COMPOSITE ENDPOINT



Win Ratio: 1.72 (1.65, 1.80)
P<0.001

QUADRUPLE GDMT USE AT OPTIMAL DOSES



Odds of optimal GDMT at 6 months Polypill vs Enhanced Usual Care:

aRR (95% CI): 1.68 (1.13 to 2.50), P = 0.011

* p<0.05

ADVERSE EVENTS

Adverse event	Polypill	Enhanced Usual Care
Serum potassium > 5.5 mmol/L	0	4
> 30% eGFR decrease	5	11
Lightheadedness or dizziness	16	6
Genitourinary infections	4	0
Permanent treatment discontinuation	4	18

KEY FINDINGS AND CLINICAL IMPLICATIONS

Among patients with HFrEF, a polypill (vs. enhanced usual care):

IMPROVED CLINICAL OUTCOMES

- **LVEF improvement:** +3.4% at 6 months
- **Hospitalizations:** 60% reduction in HF hospitalizations/ED visits

IMPROVED PATIENT-CENTERED OUTCOMES

- **Quality of life:** Meaningful improvement
- **Adherence:** 50% higher vs. usual care

IMPROVED PROCESS OF CARE

- **GDMT utilization:** Greater uptake and persistence with polypill strategy

FUTURE DIRECTIONS

- Long-term mortality and morbidity outcomes
- Implementation studies in diverse settings

THANK YOU

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