Effects of Dapagliflozin in Heart Failure Patients with Deterioration in eGFR to Less Than 25ml/min/1.73m^2: A Participant Level Pooled Analysis of the DAPA-HF and DELIVER Trials

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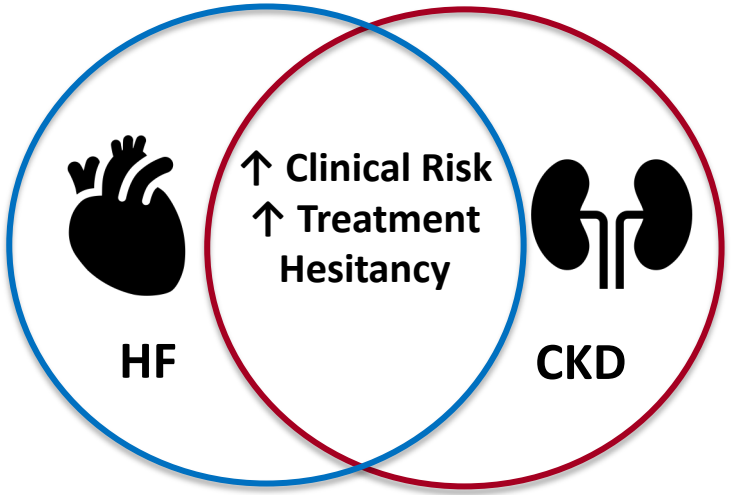
DAPAHF

DELIVER

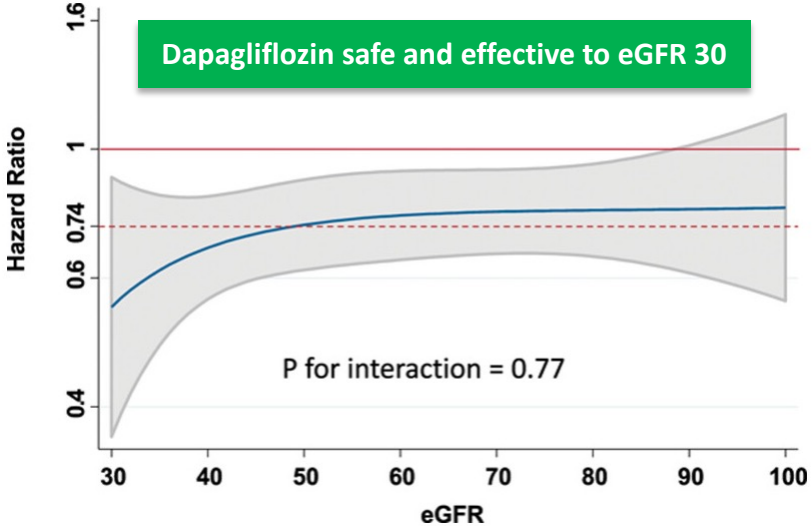
Comorbid Intersection of HF and CKD

- SGLT2 inhibitors are foundational in the management of patients with HF irrespective of LVEF
- HF and CKD frequently co-exist
- Such patients face higher risks of clinical events and progressive deterioration in kidney function
- Declines in kidney function are often associated with suboptimal HF medical therapy

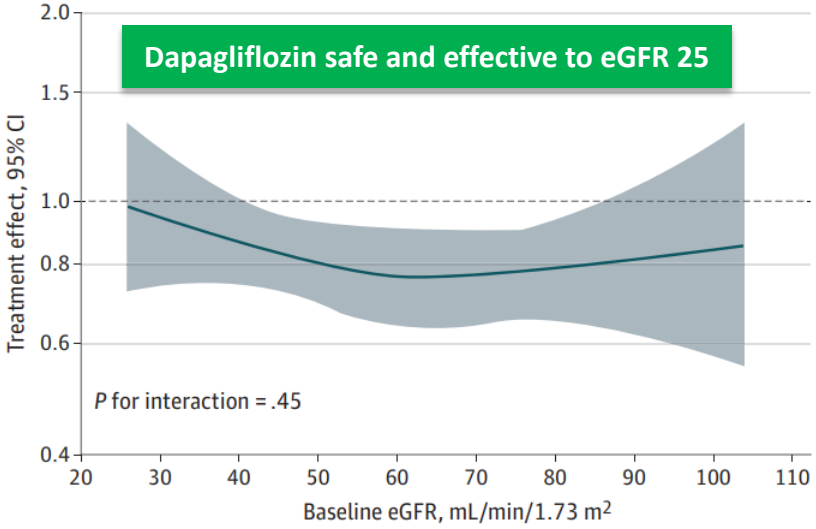


Dapagliflozin Exhibits Broad Safety and Efficacy Across Spectrum of Kidney Function

DAPA-HF



DELIVER

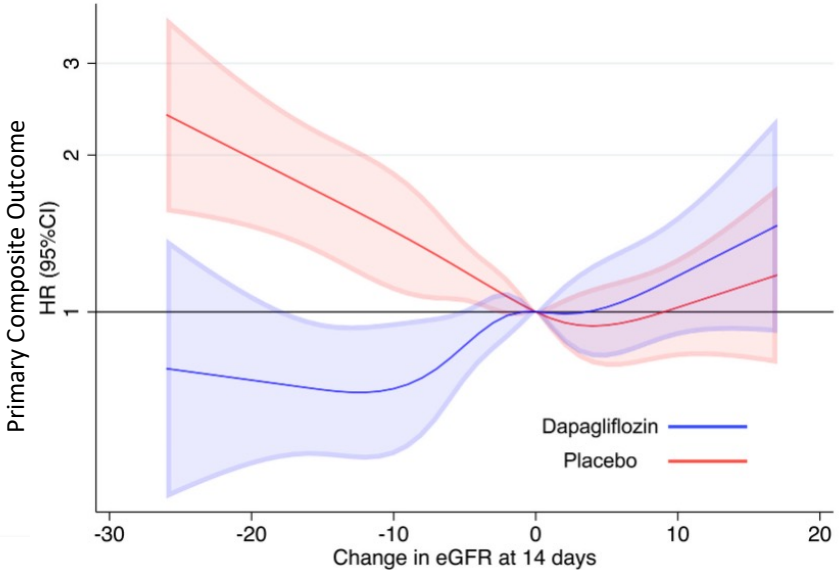


US FDA labelling does NOT recommend initiation of dapagliflozin in patients with eGFR<25ml/min/1.73m²

Jhund P, *et al.* Circulation(2020)
McCausland P, *et al.* JAMA Cardiol(2022)

Are All Declines in Renal Function the Same?

Early eGFR "dip" on Treatment Initiation

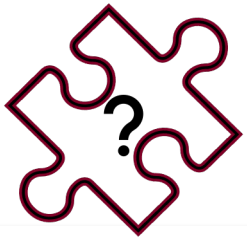


NOT adversely prognostic

Deterioration in eGFR Below Trial Inclusion Threshold

Trial	eGFR Threshold ml/min/1.73m^2	Population	Clinical Benefits
DAPA-CKD	<30	CKD	Retained
CREDENCE	<30	CKD	Retained

Heart Failure Populations



Adamson C, *et al.* Circulation(2022)
Chertow M. G, *et al*. JASN(2021)
Bakris G, *et al*. CJASN(2020)

Objectives

- Assess the frequency and prognostic implications of a deterioration in kidney function to eGFR<25ml/min/1.73m^2
- Evaluate the association between deterioration in eGFR <25ml/min/1.72m^2, treatment with dapagliflozin, and clinical efficacy and safety outcomes among patients with chronic HF

DAPA-HF Population:
NYHA II-IV, LVEF≤40%, ↑ NP or hospitalization for HF within 12 months

R

Dapagliflozin
N=2,373

Placebo
N=2,371

1º Outcome

Worsening HF or CV Death

HR 0.74; p<0.001
95% CI 0.65-0.85

DELIVER Population:
NYHA II-IV, LVEF>40%, + structural heart disease, ↑ NP

R

Dapagliflozin
N=3,131

Placebo
N=3,132

1º Outcome

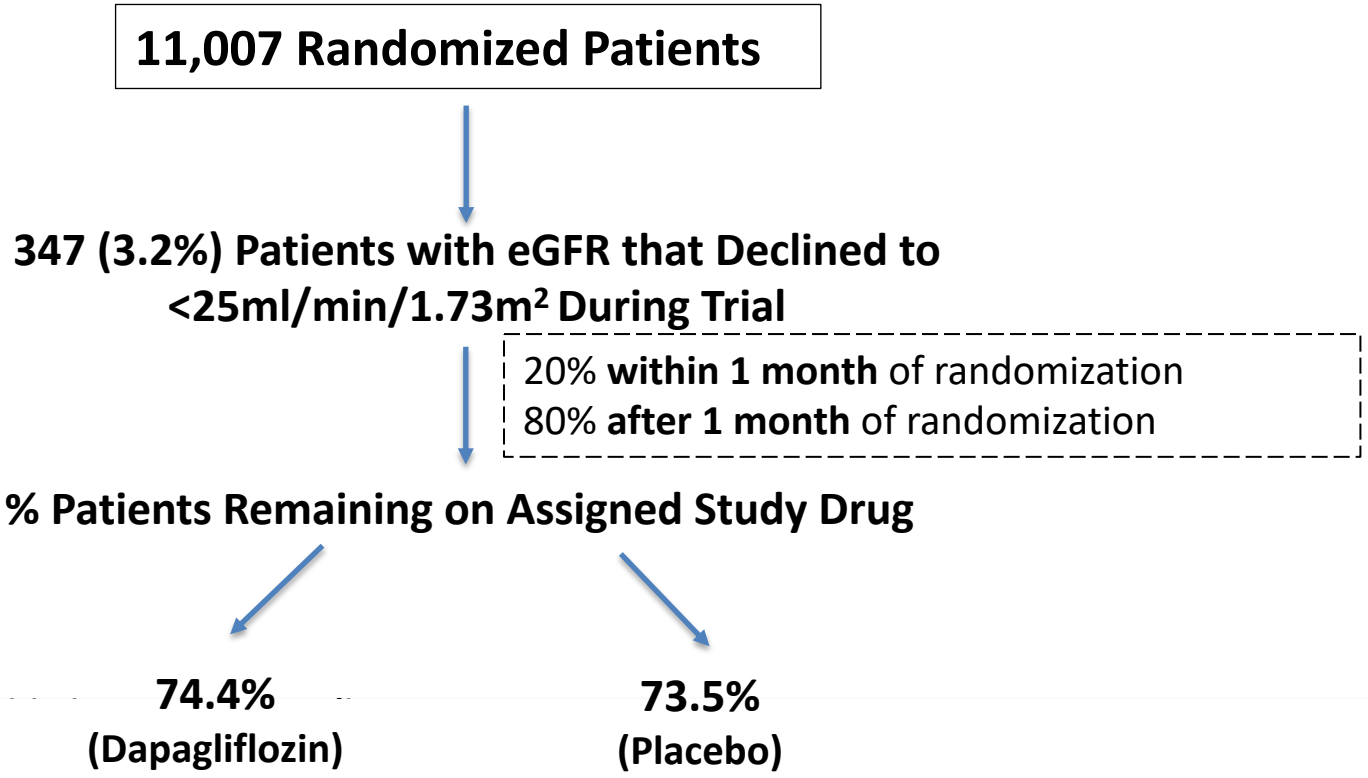
Worsening HF or CV Death

HR 0.82; p<0.001
95% CI 0.73-0.92

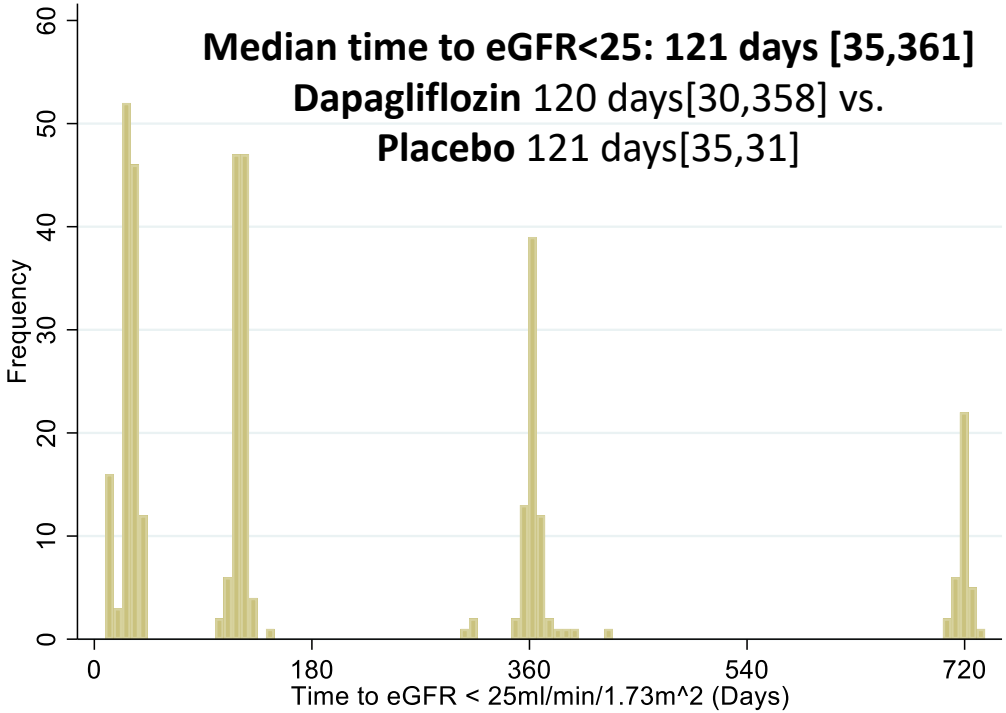
Methods

- Trial protocols did **NOT** mandate study drug discontinuation if the eGFR fell below the trial threshold for patient inclusion:
  - eGFR<30ml/min/1.73m^2 (DAPA-HF)
  - eGFR<25ml/min/1.73m^2 (DELIVER)
- We used **time updated** Cox proportional hazards models
  - Patients initially considered in a **window of risk prior to eGFR decline** below 25ml/min/1.73m^2
  - Patients **reclassified at the time of eGFR decline** below 25ml/min/1.73m^2

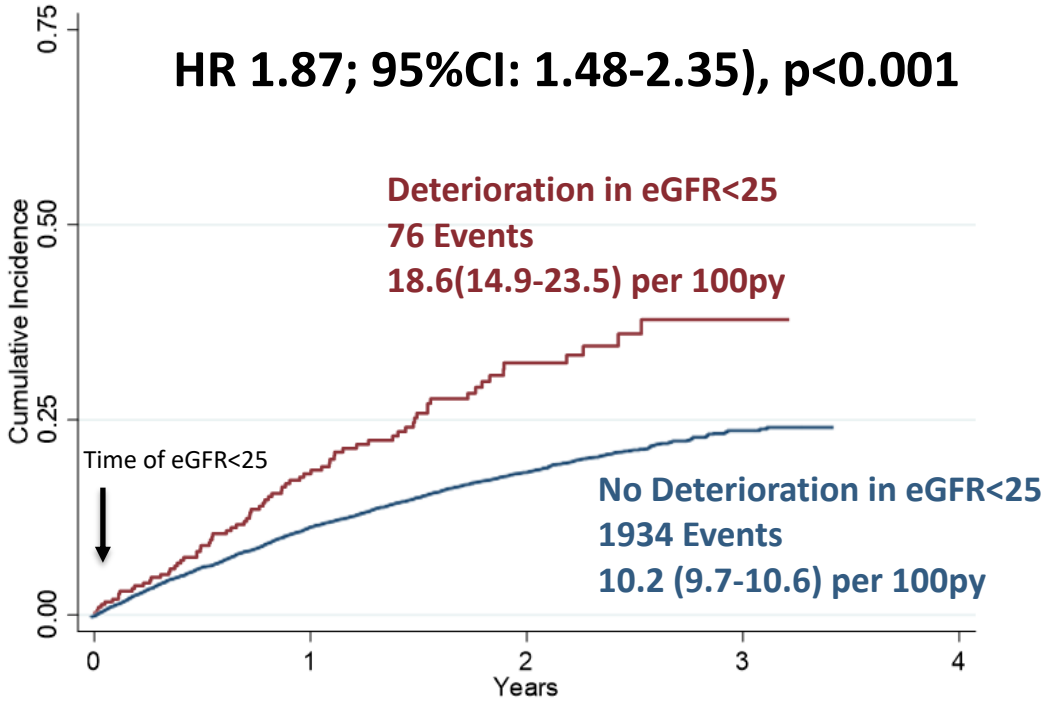
Study Flow Diagram



Distribution of Time to Deterioration in eGFR<25ml/min/1.73m^2

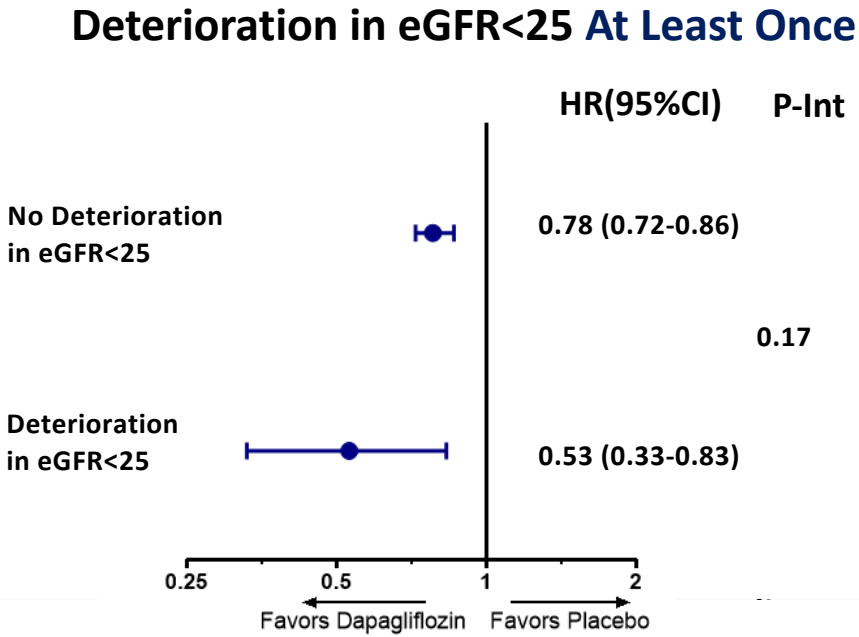


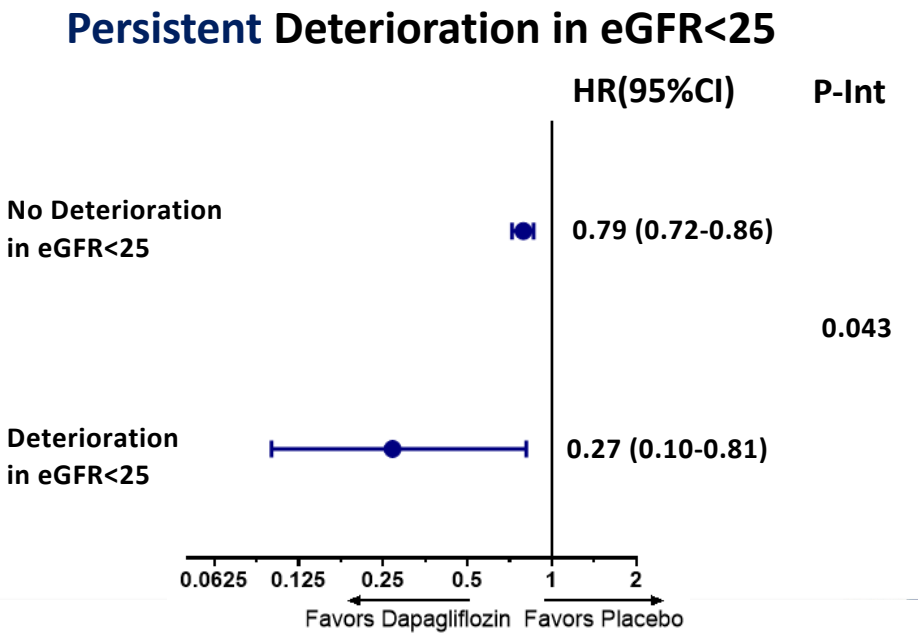
Association Between Deterioration in eGFR<25ml/min/min/1.73m^2 and Primary Composite Outcome



Analysis time for patients not experiencing deterioration in eGFR<25 was time of randomization

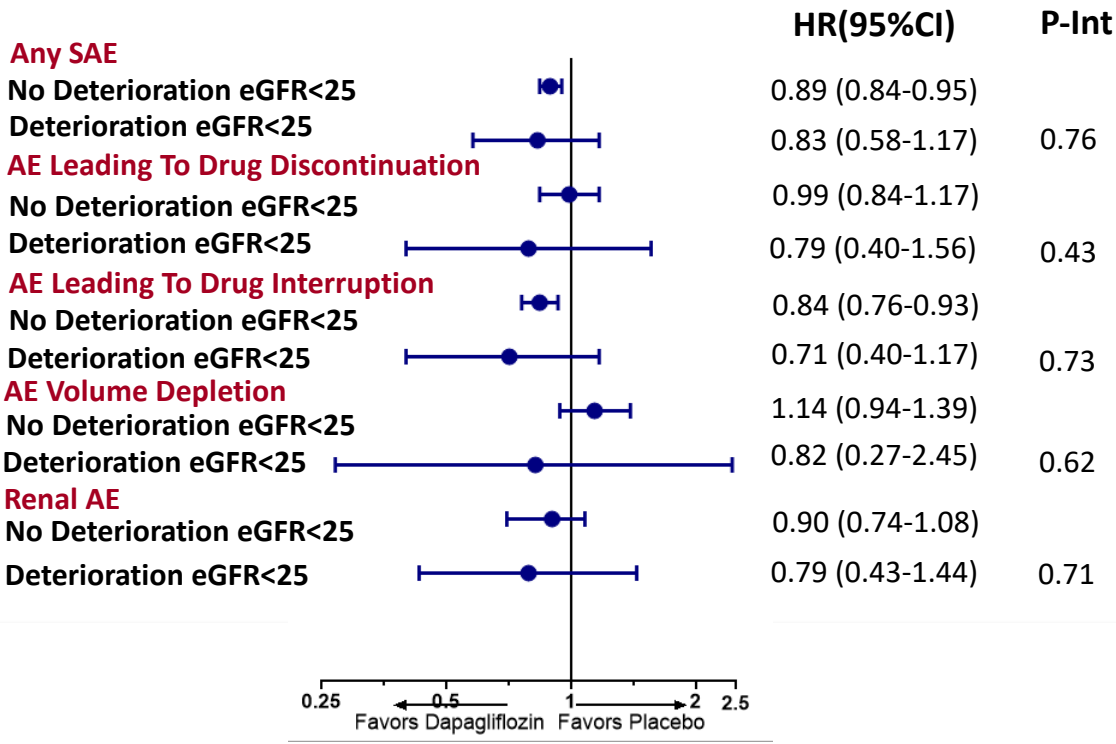
Treatment Effects of Dapagliflozin on the Primary Composite Outcome (CV Death or Worsening HF)



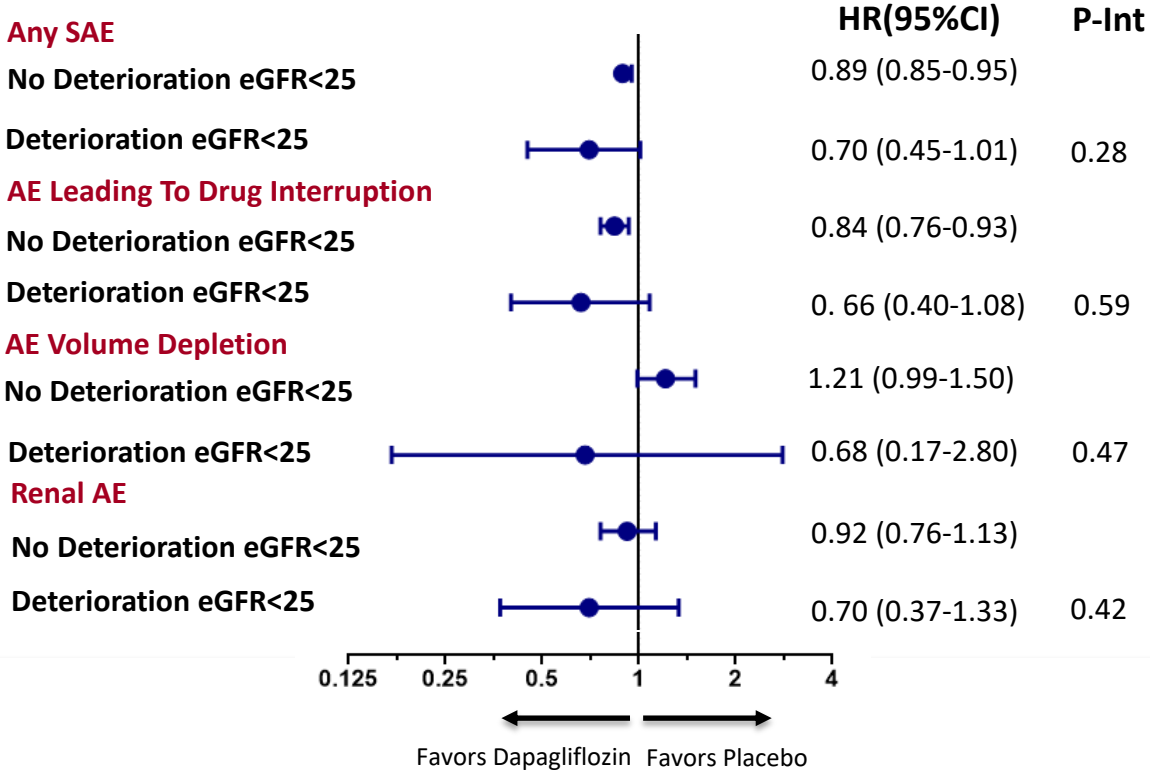


ARR 10.7 vs 2.4 per 100p-y

Treatment Effects of Dapagliflozin on the Safety Outcomes: Full Study Population



Treatment Effects of Dapagliflozin on the Safety Outcomes: Patients Remaining On Treatment



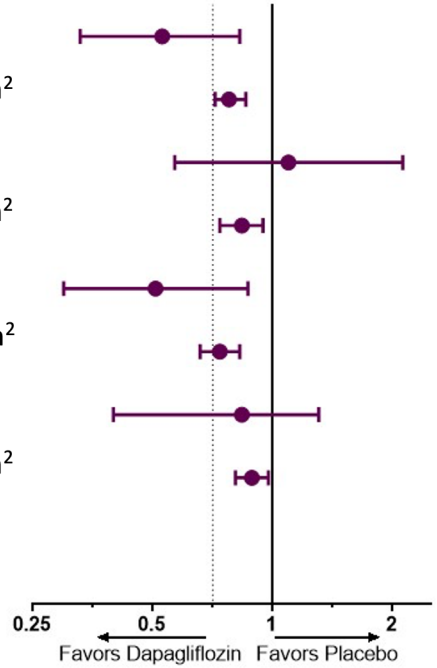
Conclusions

- Patients with HF experiencing deterioration in eGFR<25ml/min/1.73m^2 were at heightened risk for the development of subsequent CV outcomes.
- Treatment with dapagliflozin was associated with lower rates of the primary outcome regardless of deterioration of eGFR to <25ml/min/1.73m^2
- Safety of dapagliflozin appeared consistent, including among those who remained on study drug after eGFR fell to <25ml/min/1.73m^2

The benefit-to-risk ratio may favour continued treatment with dapagliflozin in patients with HF and deterioration in kidney function below eGFR 25ml/min/1.73m^2

Please visit www.delivertrial.org for more information about DELIVER

Association Between Deterioration in eGFR<25ml/min/1.73m2, Treatment with Dapagliflozin and Efficacy Outcomes



	Hazard Ratio (95%CI)	P-Interaction
Primary Composite		
Deterioration in eGFR<25 ml/min/1.73m^2	0.53(0.33-0.83)	
No Deterioration in eGFR<25 ml/min/1.73m^2	0.78(0.72-0.86)	0.17
CV Death		
Deterioration in eGFR<25 ml/min/1.73m^2	1.10 (0.57-2.13)	
No Deterioration in eGFR<25 ml/min/1.73m^2	0.84 (0.74-0.95)	0.43
HF Hospitalization		
Deterioration in eGFR<25 ml/min/1.73m^2	0.51(0.30-0.87)	
No Deterioration in eGFR<25 ml/min/1.73m^2	0.74(0.66-0.83)	0.28
All Cause Death		
Deterioration in eGFR<25 ml/min/1.73m^2	0.84(0.54-1.31)	
No Deterioration in eGFR<25 ml/min/1.73m^2	0.89(0.81-0.98)	0.85