#AHA24

GALECTIN-3 AND PROGRESSION OF KIDNEY DISEASE IN PATIENTS WITH TYPE 2 DIABETES MELLITUS:

Analyses From the DECLARE-TIMI 58 Trial

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DISCLOSURES

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BACKGROUND

- Galectin-3 is considered to be a circulating biomarker of fibrosis
- Pre-clinical studies have investigated its potentially causal role in fibrosis of the kidneys, specifically in the context of underlying kidney-damaging disease (e.g., diabetes mellitus)
- Observational studies suggest an association of Galectin-3 with kidney function and its decline in patients with established chronic kidney disease (CKD)

AIM

I. to investigate the association of galectin-3 with **decline of kidney function** in a high-risk **population (i.e. diabetes) without CKD** and

II. to investigate the **effect** of **dapagliflozin** across **galectin-3** concentrations

METHODS

- **DECLARE-TIMI 58** was a double-blind, randomized, placebo-controlled trial of dapagliflozin in patients with type 2 diabetes mellitus
- Pts were at high risk for or had established atherosclerotic cardiovascular disease
- Estimated CrCl at screening >60ml/min
- Galectin-3 (Alinity, Abbott Diagnostics) and all other biomarkers were measured at randomization
- **Primary Outcome = Kidney specific composite endpoint** adjudicated by an **independent event adjudication committee**
  - Sustained ≥40% decrease in eGFR to <60 mL/min, end-stage renal disease, or adjudicated renal death

BASELINE

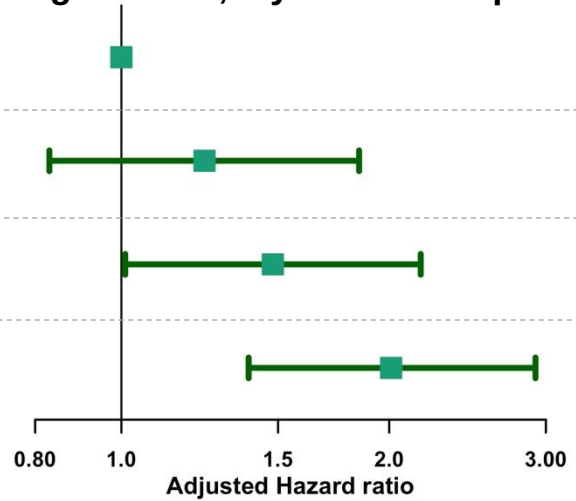
	Galectin-3 (N = 14,530)				
	Quartile 1 (N = 3,656)	Quartile 2 (N = 3,719)	Quartile 3 (N = 3,547)	Quartile 4 (N = 3,608)	P-Trend
Age (y)	62	63	64	65	<0.001
Duration of diabetes (y)	10	10	11	11	<0.001
HbA1c (%)	8.0	8.0	8.0	8.1	0.17
Baseline insulin use	39.6	39.9	43.8	42.5	<0.001
Established ASCVD	40.3	39.9	41.8	41.9	0.06
History of Heart Failure	9.4	8.9	9.9	12.2	<0.001
eGFR (CKD-EPI, ml/min)	93	90	87	81	<0.001
Urine Albumin-Creatinine-Ratio					
≥30 to ≤300mg/g	21.3	23.0	23.6	27.4	<0.001
>300mg/g	4.6	5.8	7.3	9.6	<0.001

Data in %, or median

KIDNEY ENDPOINT

Sustained ≥40% decrease in eGFR to <60 mL/min, end-stage renal disease (ESRD), or adjudicated renal death

Quartiles of galectin-3, 4-year follow-up

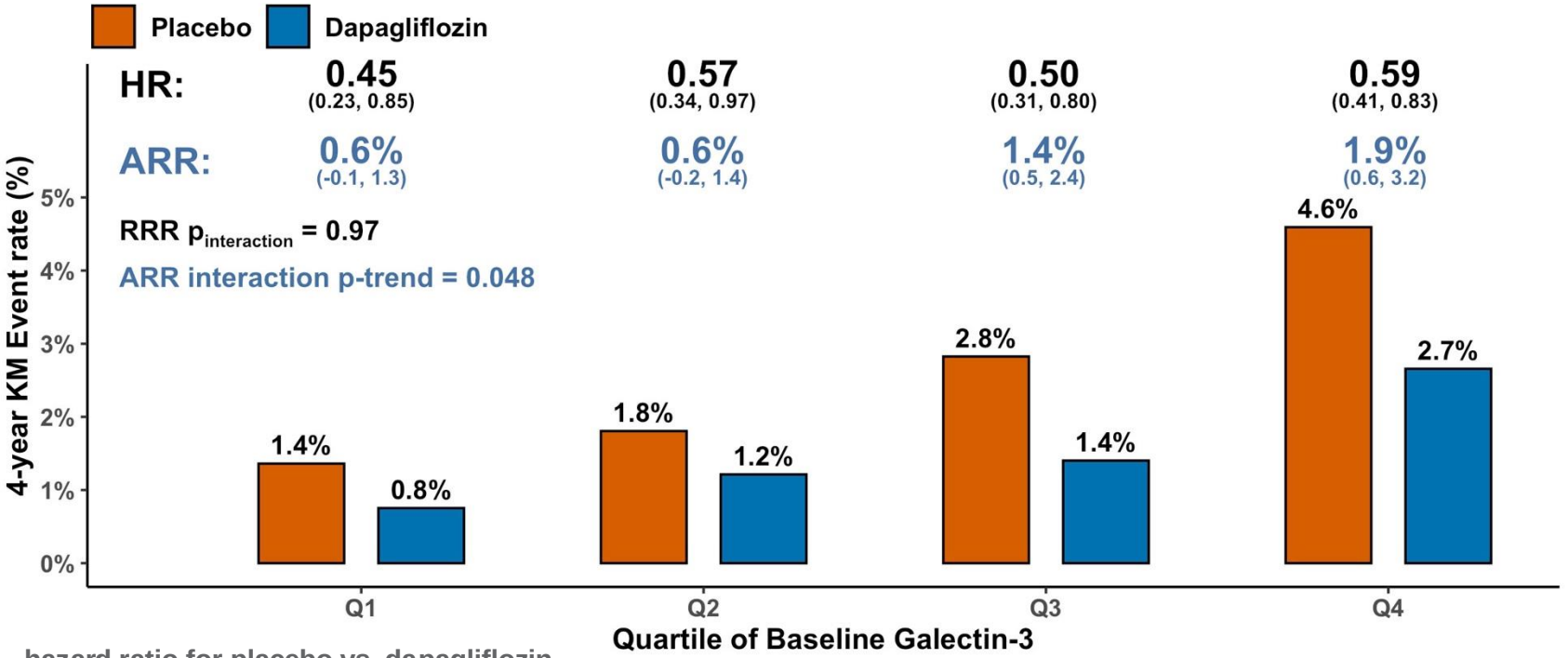


	4-year unadjusted KM rates (%)		
	eGFR decrease	**ESRD**	**Renal death**
Q1	**1.06**	**0.03**	**0**
Q2	**1.48**	**0.03**	**0**
Q3	**1.97**	**0.19**	**0.03**
Q4	**3.27**	**0.29**	**0.30**

Cox PH model adjusted for: age, sex, white race, BMI, hypertension, established CV disease, heart failure, eGFR, high-sensitivity troponin T, NT-proBNP, urine albumin-creatinine-ratio, diabetes duration

EFFICACY OF DAPAGLIFLOZIN

Sustained ≥40% decrease in eGFR to <60 mL/min, end-stage renal disease (ESRD), or adjudicated renal death



HR – hazard ratio for placebo vs. dapagliflozin

CONCLUSIONS

In patients with type 2 diabetes mellitus without CKD, galectin-3 …

- ➔ is **significantly associated with future decline in kidney function and adverse kidney outcomes**
- ➔ identifies patients with **greater absolute benefit of dapagliflozin for mitigating onset of kidney disease**

Thank you very much for your attention!