Cardiovascular Risk Stratification and Efficacy of Dapagliflozin on Cardiovascular Outcomes in Patients with T2DM in the DECLARE-TIMI 58 Trial

Kazuma Oyama,[1] Stephen D. Wiviott,[1] Itamar Raz,[2] Avivit Cahn,[2] Erica L. Goodrich[1] Deepak L. Bhatt,[1] Lawrence A. Leiter,[3] Darren K. McGuire,[4] John P.H. Wilding,[5] Ingrid A. M. Gause-Nilsson,[6] Ofri Mosenzon,[2] Marc S. Sabatine,[1] Erin A. Bohula,[1]

[1]Division of Cardiovascular Medicine, Brigham and Women's Hospital, Boston, MA
[2]Diabetes Unit, Hadassah Medical Center, Jerusalem, Israel
[3]Li Ka Shing Knowledge Institute, St. Michael's Hospital, Toronto, ON, Canada
[4]Division of Cardiology, University of Texas Southwestern Medical Center, and Parkland Health and Hospital System, Dallas, TX
[5]Institute of Ageing and Chronic Disease, University of Liverpool, Liverpool, UK
[6]Department of Internal Medicine, Seoul National University College of Medicine, Seoul, Korea
[7]Department of Cardiology, Queen Giovanna University Hospital, Sofia, Bulgaria
[8]Estudios Clínicos Latino America, Rosario, Santa Fe, Argentina
[9]Internal Cardiology Department, University Hospital Brno, Brno, Czech Republic
[10]AstraZeneca Gothenburg, Sweden

#AHA20

American Heart Association. Scientific Sessions

Disclosures

The DECLARE-TIMI 58 trial was supported by AstraZeneca.

K.O. was supported by a grant from JSPS Overseas Research Fellowships.

Background

- In DECLARE-TIMI 58, the SGLT-2 inhibitor, dapagliflozin reduced the risk of the composite of cardiovascular (CV) death or hospitalization for heart failure (HHF), and renal-specific outcomes in a broad range of patients with type 2 diabetes mellitus (T2DM).
- The TIMI Risk Score for Secondary Prevention (TRS 2°P) is a clinical risk score developed in patients with atherosclerotic cardiovascular disease (ASCVD) that provides risk stratification for MACE (CV death, MI or stroke).[1]
- We sought to investigate whether the TRS 2°P would provide risk stratification in this population for MACE as well as other endpoints, and whether dapagliflozin provides cardiac and renal protection regardless of risk.

[1]Bohula EA et al. ***Circulation*** 2016;134:304-13.

Methods

- We prospectively applied TRS 2ºP to 17,159 pts with T2DM and established ASCVD or multiple CV risk factors randomized to dapagliflozin or placebo in DECLARE-TIMI 58.
- The total risk for each pt was defined by the arithmetic sum of the number of risk indicators (RI) present (range 1-10).
- Simple risk categories were defined as low (RI=1-2), intermediate (3), and high (≥4).
- Risk stratification was assessed for the outcomes of MACE (CV death, MI or stroke), CV death/hospitalization for heart failure (HHF) and renal-specific composite outcome.

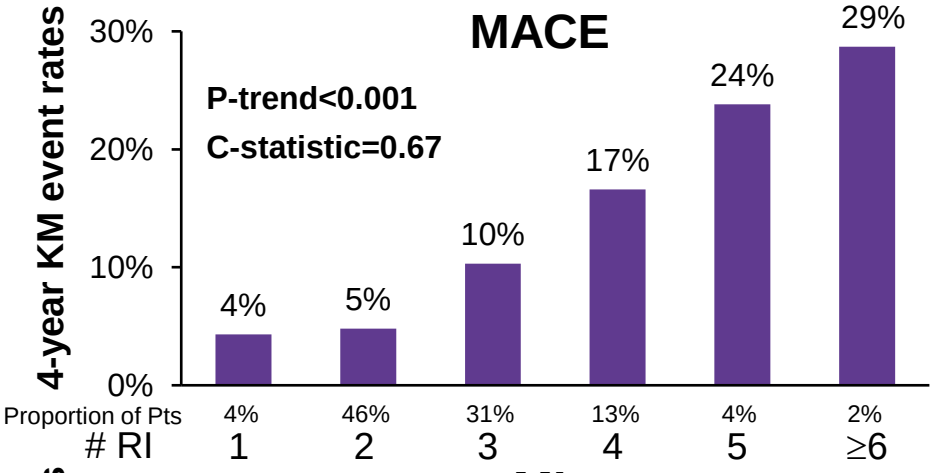
Risk Indicators	Points
Heart Failure	1
Hypertension	1
Age ≥ 75 years	1
Diabetes Mellitus	1
Prior Stroke	1
Prior CABG	1
Peripheral arterial disease	1
eGFR < 60	1
Current Smoking	1
Prior myocardial infarction	1
Max Possible	10

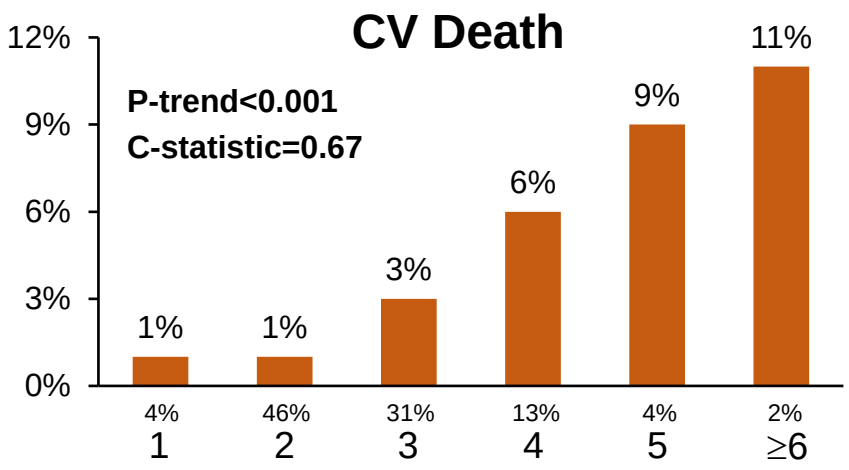
Bohula EA et al. ***Circulation*** 2016;134:304-13.
Bergmark BA et al. ***Diabetes Care*** 2018;41:577-585.

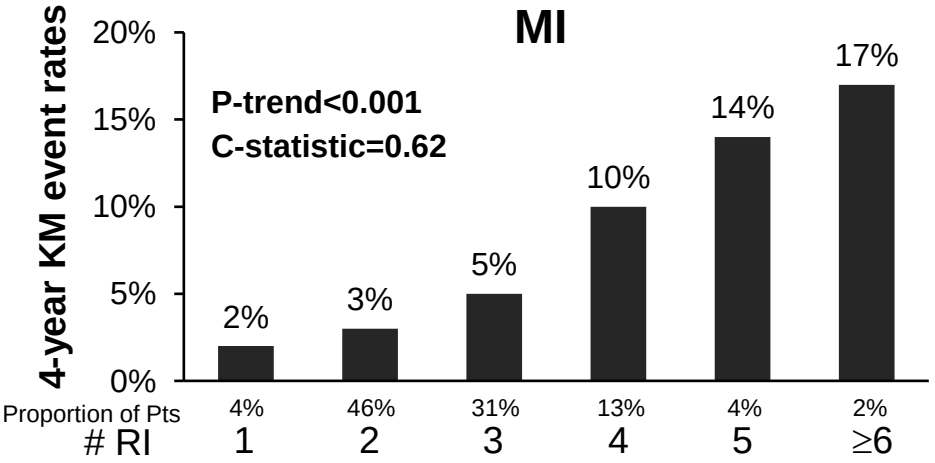
Baseline Characteristics

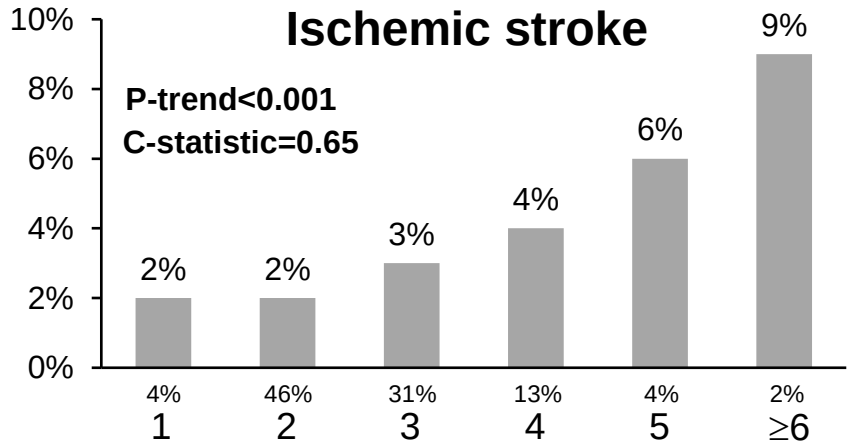
%	Low (1-2) (N=8546, 50%)	Intermediate (3) (N=5355, 31%)	High (≥4) (N=1679, 19%)
Age≥75	0.3	10	17
Female	42	36	28
Current smoking	3.1	23	30
Hypertension	84	95	97
Prior MI	2.4	25	62
Prior stroke	0.6	9.4	17
PAD	1.0	6.0	19
Prior CABG	0.6	8.8	36
History of HF	0.1	9.6	37
eGFR<60	0.3	12	27

Risk Stratification for MACE & Components by TRS 2°P in Placebo

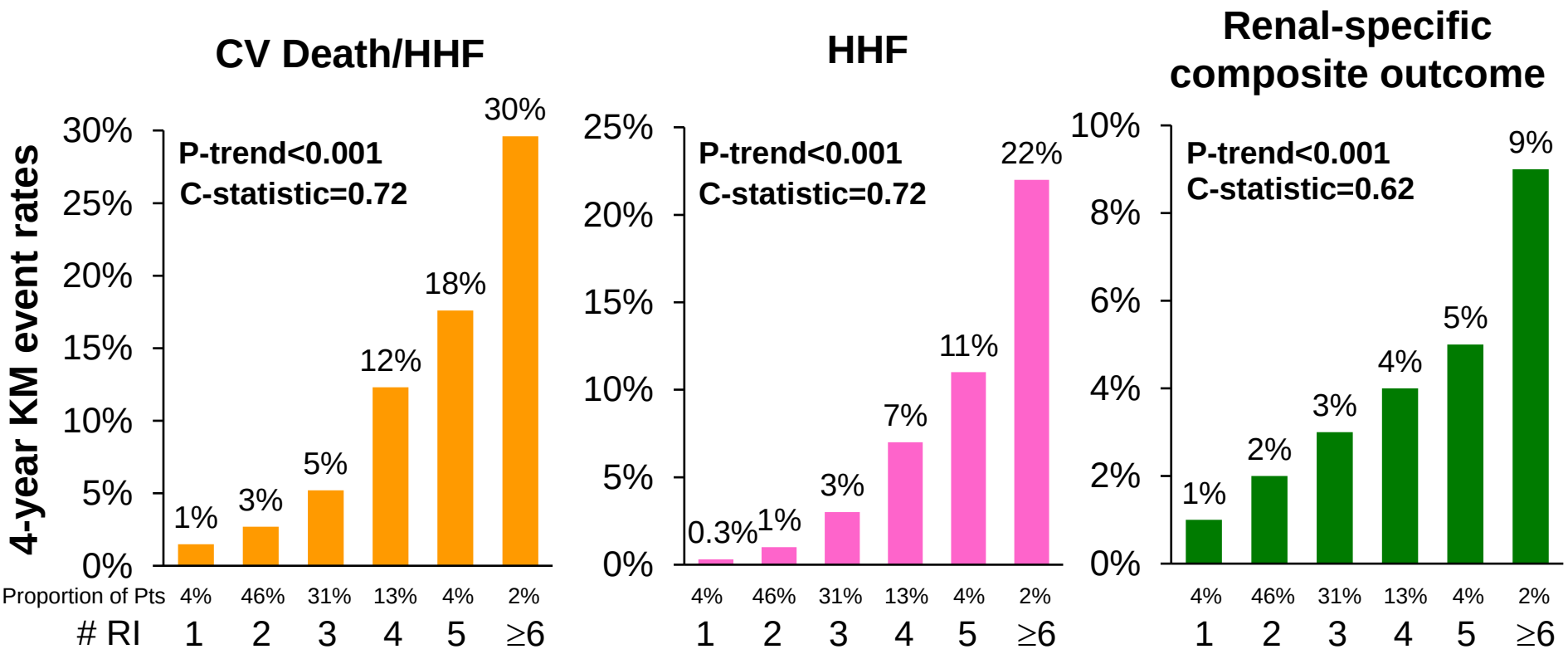








Risk Stratification by TRS 2°P for Other Endpoints in Placebo



Effect of Dapagliflozin by TRS 2°P Risk Categories

Placebo Dapagliflozin

MACE

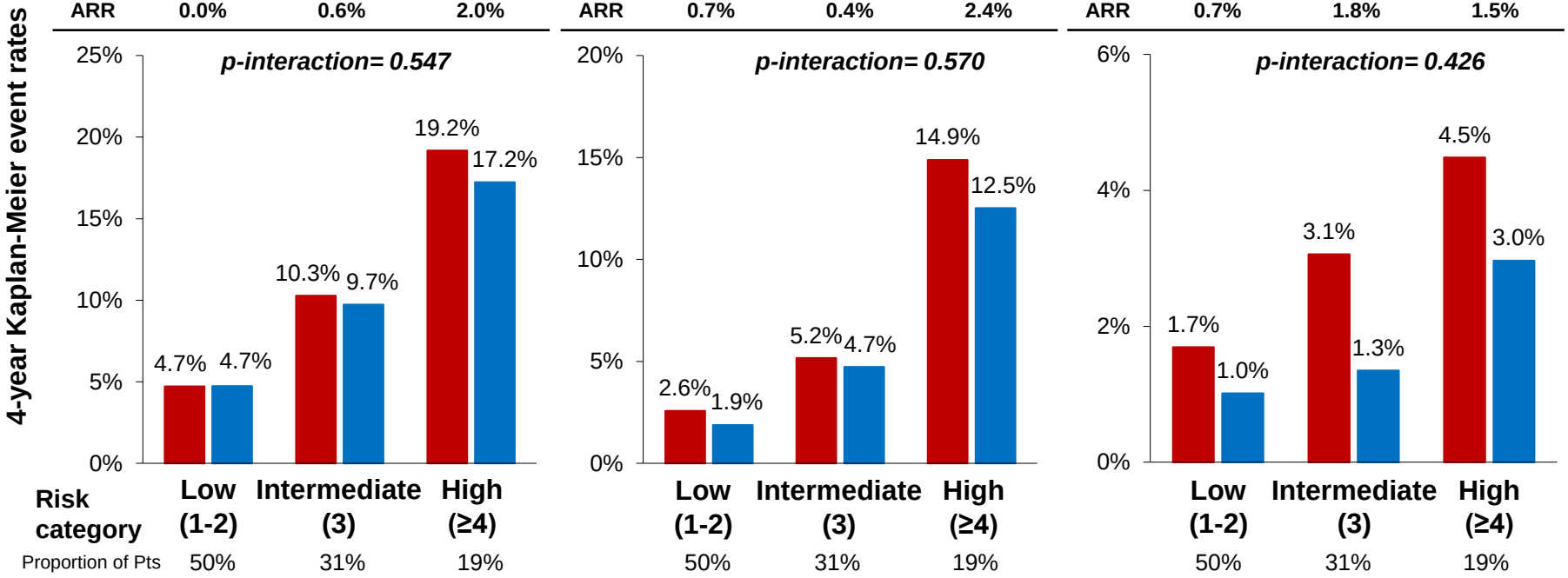
	Low	Intermediate	High
HR	1.01 (0.83-1.23)	0.93 (0.79-1.10)	0.88 (0.75-1.03)
ARR	0.0%	0.6%	2.0%

CV Death/HHF

	Low	Intermediate	High
HR	0.77 (0.58-1.02)	0.92 (0.72-1.16)	0.81 (0.67-0.97)
ARR	0.7%	0.4%	2.4%

Renal-specific composite outcome

	Low	Intermediate	High
HR	0.59 (0.41-0.85)	HR 0.43 (0.29-0.63)	0.58 (0.40-0.84)
ARR	0.7%	1.8%	1.5%



Limitations

- All patients enrolled in the DECLARE-TIMI 58 had TRS 2°P>0 because they all had T2DM at baseline.
- TRS 2°P was composed of readily available clinical data without other possible risk indicators (e.g. imaging, angiography, biochemical or genetic characteristics) that may provide additional refinement for stratification.

Conclusion

Cardiovascular risk stratification using TRS 2°P identifies patients with T2DM at high risk of MACE, as well as CV death/HHF and renal-specific outcomes. Relative reductions with dapagliflozin for CV death/HHF and renal-specific outcomes were consistent across the range of TRS 2°P and the absolute risk reduction tended to be greatest in the highest risk group.