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Diabetes treatment lowers PromarkerD risk score: Results presented at Australasian Diabetes Congress

Proteomics International Laboratories Ltd (Proteomics International; ASX: PIQ) is pleased to provide a copy of its conference presentation to the Australasian Diabetes Congress in Brisbane, 11-13 August 2021, titled "*Canagliflozin attenuates PromarkerD diabetic kidney disease risk prediction scores*".

The conference abstract describing this study (design, results and conclusion) was released ahead of the conference [ASX: 16 July]. The presentation also states that further analysis will now be conducted to refine the statistical modelling used in the study, and to assess the prognostic utility of change in PromarkerD scores over time for predicting future renal outcomes.

Australasian Diabetes Congress presentation (ID: 27; Track: ADS Clinical ePosters)
[See attached presentation]
Titled: *Canagliflozin attenuates PromarkerD diabetic kidney disease risk prediction scores*

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Authorised by the Board of Proteomics International Laboratories Ltd (ASX.PIQ).

ENDS

About Diabetes and Diabetic Kidney Disease
Type 2 diabetes is a global health problem affecting 463 million adults worldwide [1]. Diabetes can cause serious and life-threatening complications, including diabetic kidney disease (DKD), a chronic and progressive kidney disease that if unchecked can lead to end stage renal disease (ESRD) resulting in dialysis or kidney transplant. Currently, 1-in-3 adults with diabetes are estimated to have DKD [2]. Diabetes is the leading cause of kidney disease in the United States and 39% of ESRD cases are attributable to diabetes [2]. Diabetes-associated chronic kidney disease is the 16th leading cause of death in the US, accounting for 40,000 deaths per year [3]. Average treatment costs for dialysis are $72,000 per person per year, with kidney disease and ESRD costing US Medicare $130 billion annually [4]. The current gold standard diagnostic tests for DKD are the urinary albumin-to-creatinine ratio (uACR ≥30 mg/g) and reduced estimated glomerular filtration rate (eGFR <60 mL/min/1.73m^2). Both these tests lack precision and sensitivity [5] and, critically, they have limited performance in predicting future decline in renal function [6].

About PromarkerD (www.PromarkerD.com)
Diabetic kidney disease (DKD) is a serious complication arising from diabetes which if unchecked can lead to dialysis or kidney transplant. PromarkerD is a prognostic test that can predict future kidney function decline in patients with type 2 diabetes and no existing DKD. The patented PromarkerD test system uses a simple blood test to detect a unique 'fingerprint' of the early onset of the disease by measuring three serum protein biomarkers, combined with three routinely available conventional

clinical variables (age, HDL-cholesterol and estimated glomerular filtration rate (eGFR)) [7]. In clinical studies published in leading journals PromarkerD correctly predicted up to 86% of otherwise healthy diabetics who went on to develop diabetic kidney disease within four years [8, 9]. The PromarkerD test is CE Mark registered in the European Union.

Further information is available through the PromarkerD web portal.

To visit the PromarkerD virtual booth please see: www.PromarkerD.com/product

[1] International Diabetes Federation Diabetes Atlas 2019.
[2] Centers for Disease Control and Prevention. Chronic Kidney Disease National Facts 2021.
[3] Mokdad AH et al. The State of US Health, 1990-2016: Burden of Diseases, Injuries, and Risk Factors Among US States. JAMA 2018
[4] United States Renal Data System 2020 Annual Data Report.
[5] Kidney Disease: Improving Global Outcomes Chronic Kidney Disease Guideline Development Work Group, M. KDIGO 2012 Clinical practice guideline for the evaluation and management of chronic kidney disease. Kidney Int. Suppl. 2013.
[6] Dunkler, D et al, R. Risk Prediction for Early CKD in Type 2 Diabetes. Clin. J. Am. Soc. Nephrol. 2015.
[7] Peters KE et al. Identification of Novel Circulating Biomarkers Predicting Rapid Decline in Renal Function in Type 2 Diabetes: The Fremantle Diabetes Study Phase II. Diabetes Care. 2017.
[8] Peters KE et al. PromarkerD Predicts Renal Function Decline in Type 2 Diabetes in the Canagliflozin Cardiovascular Assessment Study (CANVAS). Journal of Clinical Medicine. 2020.
[9] Peters KE et al. Validation of a Protein Biomarker Test for Predicting Renal Decline in Type 2 Diabetes: The Fremantle Diabetes Study Phase II. J Diab Comp. 2019.

About Proteomics International Laboratories (PILL) (www.proteomicsinternational.com)
Proteomics International (Perth, Western Australia) is a wholly owned subsidiary and trading name of PILL (ASX: PIQ), a medical technology company at the forefront of predictive diagnostics and bio-analytical services. The Company specialises in the area of proteomics – the industrial scale study of the structure and function of proteins. Proteomics International's mission is to improve the quality of lives by the creation and application of innovative tools that enable the improved treatment of disease.

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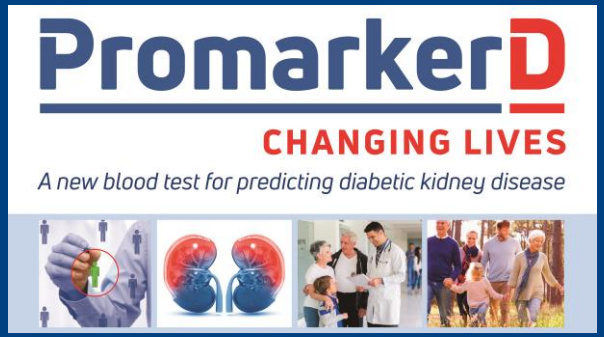
Proteomics International

CANVAS Program



Canagliflozin attenuates PromarkerD diabetic kidney disease risk prediction scores

Kirsten E. Peters[1,2], Katrina Spilsbury[1], Jialin Xu[3], Scott D. Bringans[1], Timothy M.E. Davis[2], Norman Rosenthal[3], Michael K. Hansen[3], Richard J. Lipscombe[1]

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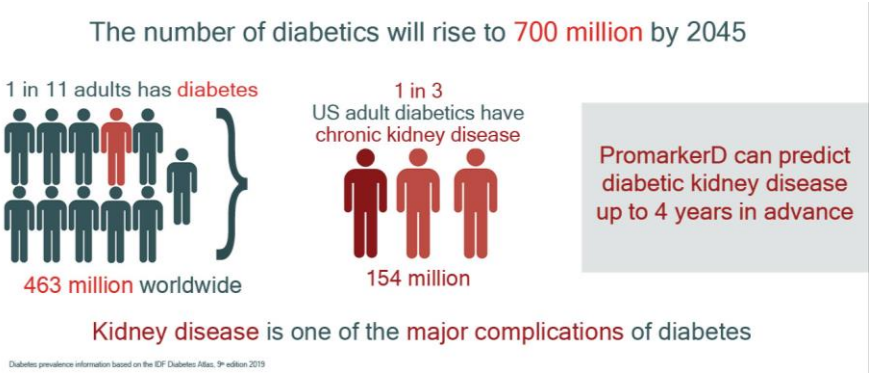
Poster 27
August 11-13th, 2021

Disclosures: This study was funded by Proteomics International. PromarkerD biomarker concentrations and risk scores were measured using archived samples from the CANVAS study by Proteomics International using a patented test owned by the company. The CANVAS study was funded by Janssen Research & Development, LLC. Canagliflozin has been developed by Janssen Research & Development, LLC, in collaboration with Mitsubishi Tanabe Pharma Corporation.

Background & Aim

- Diabetic kidney disease (DKD) is the leading cause of end-stage renal disease.[1]
- PromarkerD is a simple biomarker-based blood test that can predict future renal function decline in individuals with T2D and no existing DKD (eGFR ≥60 mL/min/1.73m^2).[2,3]
- Canagliflozin (CANA), a sodium glucose transporter subtype 2 (SGLT-2) inhibitor, is approved for blood glucose lowering in T2D, and for risk reduction of renal and cardiovascular outcomes.[4]
- The effect of CANA on PromarkerD scores is unknown.



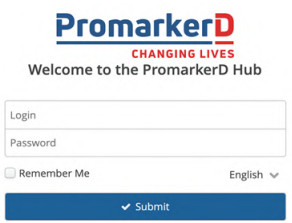
- The aim of this study was to examine the association between CANA and change in PromarkerD risk score over a three-year follow-up period in patients with T2D participating in the CANagliflozin cardioVascular Assessment Study (CANVAS).

[1] https://www.cdc.gov/kidneydisease/pdf/Chronic-Kidney-Disease-in-the-US-2021-h.pdf, [2] Peters et al., Diab Care. 2017;40:1548-1555, [3] Peters et al., J Diab Comp. 2019;33:107406, [4] Neal et al., N Eng J Med. 2017;377(7):644-657.

Methods

- PromarkerD scores were measured at baseline (Yr0) and Yr3 in 2,008 T2D participants without DKD[#] (n=629 placebo/n=1,379 CANA, mean age 62 years, 69% males, median diabetes duration 12 years).[1]
- PromarkerD scores combine 3 protein biomarker concentrations (CD5L, ApoA4, IGFBP3) with clinical data (age, serum HDL-cholesterol, eGFR*), and are categorised as low-, moderate- or high-risk for renal outcomes.
- Generalized estimating equations were used to assess the effect of canagliflozin versus placebo on PromarkerD scores, with effects assessed by baseline PromarkerD risk category.

Samples (Yr0+Yr3) → **Biomarkers by IVD** → **Clinical Factors** → **PromarkerD Hub** → **PromarkerD Result**



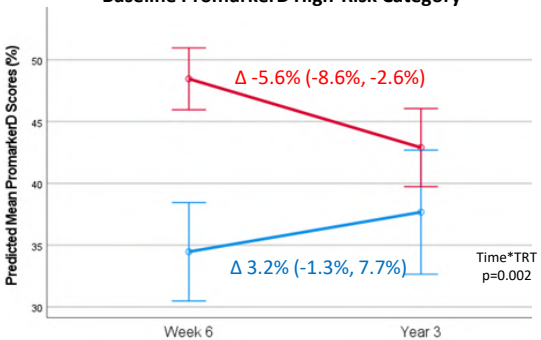
[1] Peters et al., J Clin Med. 2020;9(10):3212, [#] DKD defined as eGFR<60mL/min/1.73m^2, * Week 6 eGFR was used in Yr0 PromarkerD scores to account for the known acute drop in eGFR following CANA initiation (Oshima et al., JASN. 2020;31(10):2446); 52 individuals were missing a week 6 eGFR and were excluded.

ΔPromarkerD Scores by PromarkerD Risk Category

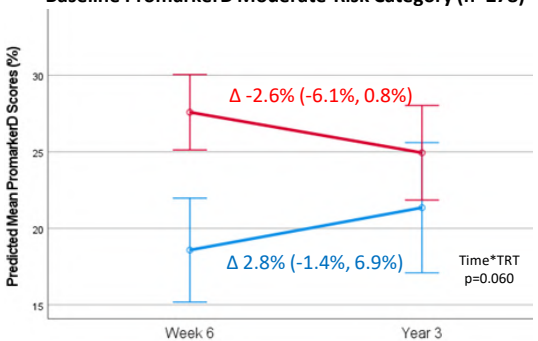
Placebo
Cana 100+300 mg

- Across all participants, those on **canagliflozin** had **decreased mean PromarkerD scores** (Δ score: -1.0% (-1.9%, -0.1%); p=0.038), while those on **placebo increased** over the three-year period (Δ score: 3.9% (2.5%, 5.3%); p<0.001). The effect was greatest for participants in the PromarkerD high-risk category:

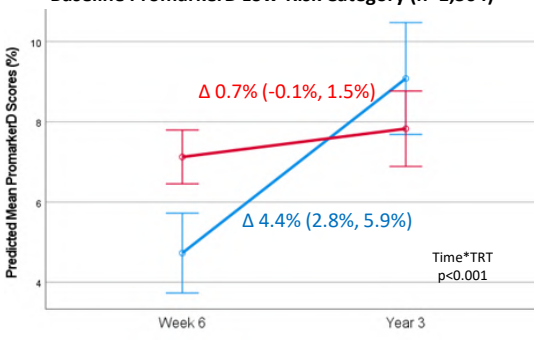
Baseline PromarkerD High-Risk Category



Baseline PromarkerD Moderate-Risk Category (n=278)



Baseline PromarkerD Low-Risk Category (n=1,304)



PromarkerD High-Risk (Time*TRT p=0.002)	N	Mean	95%CI	Difference in the means Δ ProD	95%CI	p-value
Difference in ProD scores between treatment arms						
Week 6						
Placebo	106	34.5	30.9, 38.0	ref		
Canagliflozin	268	48.5	45.8, 51.1	14.0	9.3, 18.7	<0.001
Year 3						
Placebo	106	37.7	33.2, 42.1	ref		
Canagliflozin	268	42.9	39.6, 46.2	5.2	-0.7, 11.2	0.084
Difference in ProD scores between Week 6 and Year 3 for						
Placebo						
Week 6	106	34.5	30.9, 38.0	ref		
Year 3	106	37.7	33.2, 42.1	3.2	-1.4, 7.8	0.17
Canagliflozin						
Week 6	268	48.5	45.8, 51.1	ref		
Year 3	268	42.9	39.6, 46.2	-5.6	-8.6, -2.5	<0.001

PromarkerD Moderate-Risk (Time*TRT p=0.060)	N	Mean	95%CI	Differences in the means Δ ProD	95%CI	p-value
Difference in ProD scores between treatment arms						
Week 6						
Placebo	96	18.6	15.3, 21.9	ref		
Canagliflozin	182	27.6	25.1, 30.1	9.0	4.8, 13.2	<0.001
Year 3						
Placebo	96	21.3	17.0, 25.7	ref		
Canagliflozin	182	24.9	21.9, 28.0	3.6	-1.7, 8.9	0.18
Difference in ProD scores between Week 6 and Year 3 for						
Placebo						
Week 6	96	18.6	15.3, 21.9	ref		
Year 3	96	21.3	17.0, 25.7	2.8	-1.4, 6.9	0.19
Canagliflozin						
Week 6	182	27.6	25.1, 30.1	ref		
Year 3	182	24.9	21.9, 28.0	-2.6	-6.1, 0.8	0.14

PromarkerD Low-Risk (Time*TRT p<0.001)	N	Mean	95%CI	Differences in the means Δ ProD	95%CI	p-value
Difference in ProD scores between treatment arms						
Week 6						
Placebo	408	4.7	4.0, 5.5	ref		
Canagliflozin	896	7.1	6.4, 7.9	2.4	1.2, 3.6	<0.001
Year 3						
Placebo	408	9.1	7.4, 10.7	ref		
Canagliflozin	896	7.8	7.0, 8.7	-1.3	-2.9, 0.4	0.15
Difference in ProD scores between Week 6 and Year 3 for						
Placebo						
Week 6	408	4.7	4.0, 5.5	ref		
Year 3	408	9.1	7.4, 10.7	4.4	2.8, 5.9	<0.001
Canagliflozin						
Week 6	896	7.1	6.4, 7.9	ref		
Year 3	896	7.8	7.0, 8.7	0.7	-0.1, 1.5	0.091

ProD=PromarkerD, TRT=treatment, * Week 6 eGFR was used in Yr0 PromarkerD scores to account for the known acute drop in eGFR following CANA initiation (Oshima et al., JASN. 2020;31(10):2446); 52 individuals were missing a week 6 eGFR and were excluded.

Conclusions

- This post-hoc analysis of data from 2,008 CANVAS participants with T2D and no DKD showed:
  - Canagliflozin significantly lowered mean PromarkerD scores compared to placebo over 3 years.
  - The greatest effect of canagliflozin was in those classified by PromarkerD as at high-risk of a subsequent decline in renal function.
  - PromarkerD can identify patients who are asymptomatic for DKD, and canagliflozin improves the associated PromarkerD renal risk profiles.
  - Follow-up PromarkerD testing would support cost effective individualised treatment via
    - Early introduction of preventative medications in high-risk patients, and
    - Rationalised treatment options in low-risk patients.

- Additional analyses are underway to:
  - Develop adjusted models for patients already on an SGLT2i, given the known transient acute drop in eGFR following treatment initiation. This will allow patients already on an SGLT2i to have the PromarkerD test and understand future risk of renal outcomes.
  - Assess the prognostic utility of change in PromarkerD scores over time for predicting future renal outcomes.