APCN x TSN 2025
23rd Asian Pacific Congress of Nephrology
Gene, Immunology, Vast, MEtabolism at its Finest!
2025 Dec. 5 Fri. ▶ 7 Sun.
TaiNEX 2, Taipei, Taiwan

Oral **S**emaglutide Use in the Real **WO**rld, Multi-Centre Experience on **R**enal Outcomes of **D**iabetic Kidney Disease in Malaysia (**SWORD**)

Jun Min Em[1], Mifzal Al Khair[2], Chew Ming Wong[2,4], Lee Ling Lim[3], R. Jeyakantha Ratnasingam[3], Rosnawati Yayha[5], Shiong Shiong Yew[6], Yok Wai Chow[7], Tee Chau Keng[8], Chong Men Leong[9], Azreen Syazril Adnan[11], Eng Khim Ng[5], Yeong Woei Chiew[5], Li Ping Tan[11], Yip Boon Chong[10], Wai Yew Kong[12], Rashidi Saidin[13], Soo Kun Lim[2,4]

[1]Division of Nephrology, Medical Department, University Malaya Medical Centre, Kuala Lumpur, Malaysia
[2]Division of Nephrology, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia
[3]Division of Endocrinology, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia
[4]Department of Nephrology, University Malaya Specialist Centre, Kuala Lumpur, Malaysia
[5]Department of Nephrology, Sunway Medical Centre, Kuala Lumpur, Malaysia
[6]Department of Nephrology, Mahkota Medical Centre, Melaka, Malaysia
[7]Department of Nephrology, Pantai Hospital, Ayer Keroh, Melaka, Malaysia
[8]Department of Nephrology, Thomson Hospital, Kota Damansara, Selangor, Malaysia
[9]Department of Nephrology, Sunway Medical Centre, Penang, Malaysia
[10]Department of Nephrology, Sunway Medical Centre, Damansara, Selangor, Malaysia
[11]Department of Nephrology, Ara Damansara Medical Centre, Selangor, Malaysia
[12]Department of Nephrology, Bukit Tinggi Medical Centre, Selangor, Malaysia
[13]Department of Nephrology, Avisena Renal Care, Shah Alam, Selangor, Malaysia

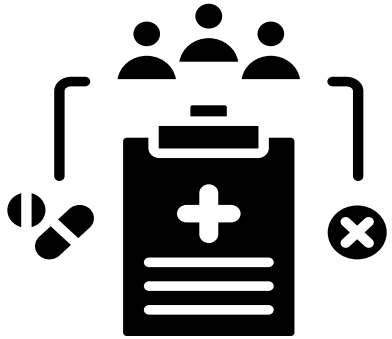
SWORD TRIAL

Introduction

- TARGET-T2D[1]: 29.8% of DM patients have CKD, 58.6% have UACR >3mg/mmol.
- Diabetic kidney disease (DKD) is the highest leading cause (56.3%) of end-stage kidney disease (ESKD)[2].
- Semaglutide improved glycaemic control and reduce cardiovascular events in type 2 diabetes (T2DM) patients in the SOUL[3] trial, positive renal outcomes in FLOW[4] trial. However, primary kidney outcomes are not studied in the oral formulation.
- This study aims to evaluate oral Semaglutide real-world effectiveness, safety, and kidney outcomes in DKD patients.

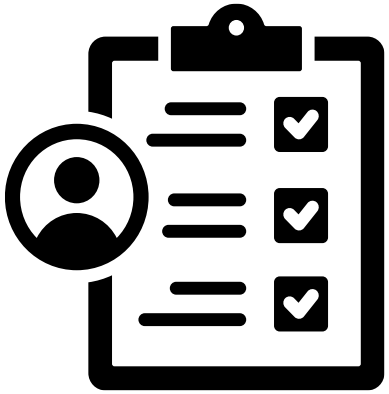
1. Lim et al. Real-world evaluation of care for type 2 diabetes in Malaysia: A cross-sectional analysis of the treatment adherence to guideline evaluation in type 2 diabetes (TARGET-T2D) study. *PloS one*, *19*(1), e0296298. https://doi.org/10.1371/journal.pone.0296298
2. Dialysis in Malaysia. 31st Malaysian Dialysis and Transplant Registry (2023)
3. Perkovic et al. FLOW Trial Committees and Investigators (2024). Effects of Semaglutide on Chronic Kidney Disease in Patients with Type 2 Diabetes. *The New England journal of medicine*, *391*(2), 109–121. https://doi.org/10.1056/NEJMoa2403347
4. McGuire et al. SOUL Study Group (2025). Oral Semaglutide and Cardiovascular Outcomes in High-Risk Type 2 Diabetes. *The New England journal of medicine*, *392*(20), 2001–2012. https://doi.org/10.1056/NEJMoa2501006

Methodology



Prospective,
Observational study

11 Malaysian Hospitals



- Adult T2DM adults (≥18 years old) with Diabetic kidney disease (DKD)
- Prescribed oral Semaglutide for at least six months

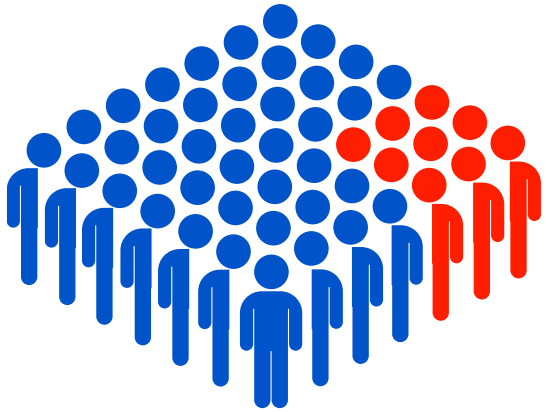
- Non-diabetic or T1DM
- Known ESKD prior to recruitment
- History of GLP-1Ra intolerance
- Significant co-morbidities that could affect renal outcomes

Methodology

Data Management

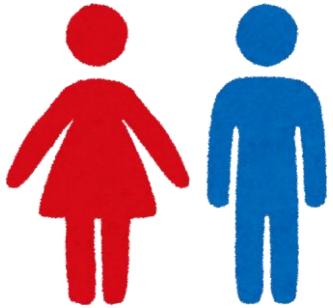
- Data collection on clinical status and biochemical parameters are collected at baseline, 6, 12 and 24 months from the oral Semaglutide initiation
- Recruitment starting from Feb 1, 2023
- Interim analyses until April 30, 2025
- Data analysis performed using SPSS version 29.0.2
  - Parametric vs. non-parametric analyses are performed based on the data distribution
- Data presentation
  - Linear graphs for parameter trend
  - Sankey diagram for albuminuria changes

Baseline Characteristics

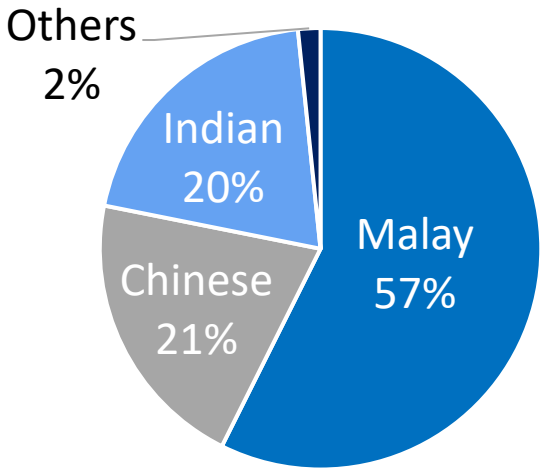


Population
Screened: 562
Recruited: **366**

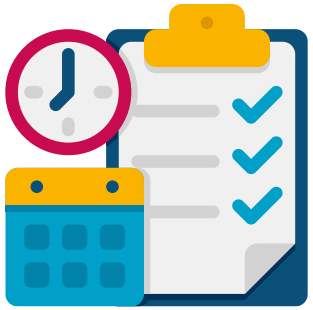
Mean Age
57.5 ± 12.4 years



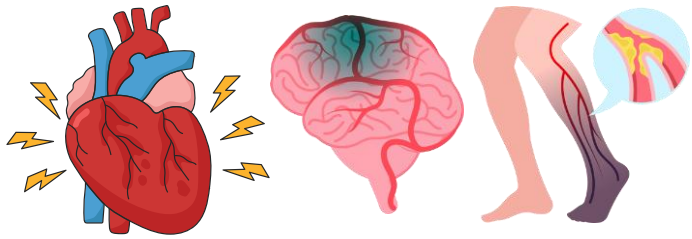
Female vs. Male
51.9% 48.1%



Race



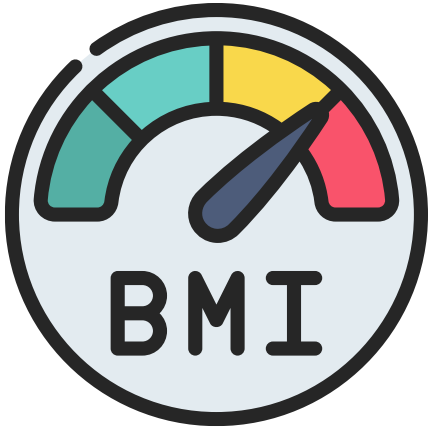
Mean T2DM duration
14.8 ± 10.0 years



Pre-existing ASCVD
(23.5%)

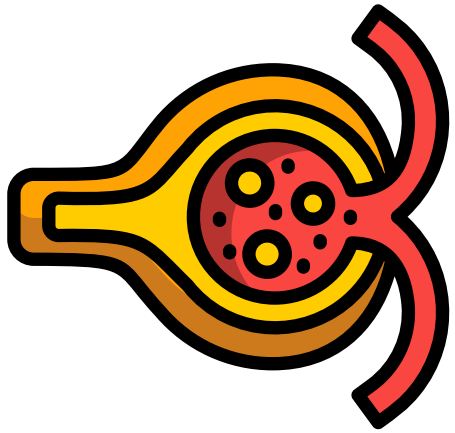
Pre-existing Heart Failure
(3.6%)

Baseline Characteristics



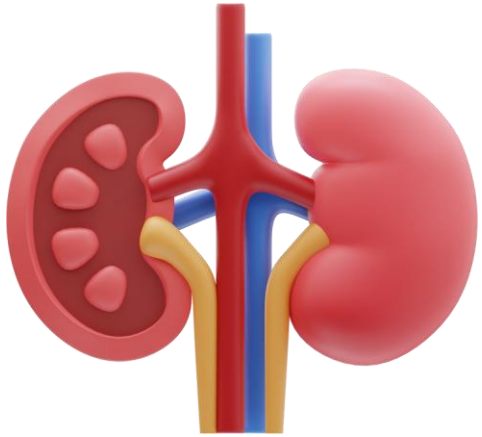
Mean Body Mass Index (BMI)

33.2 ± 7.5 kg/m^2



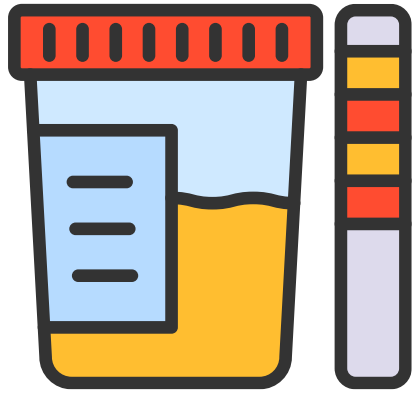
Mean Serum Creatinine

102.8 ± 56.4 µmol/L



Mean estimated GFR

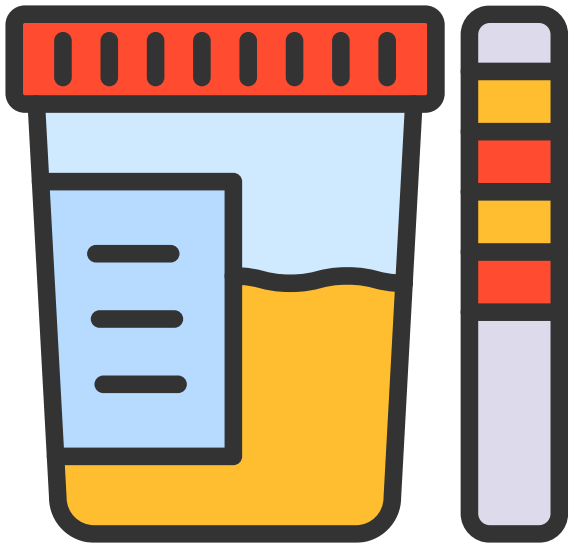
80.1 ± 37.4 ml/min/1.72m^2



Median UACR

9.40 mg/mmol (IQR 52.7)

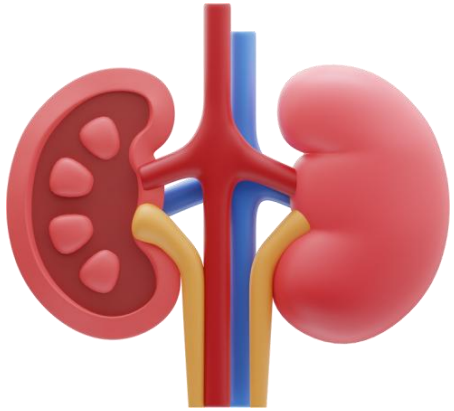
Baseline Characteristics

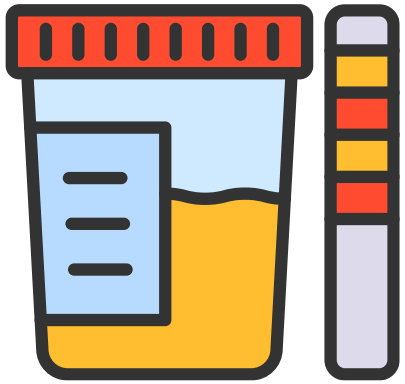


UACR Category	N (%)
A1 (<3 mg/mmol)	**110 (31.5%)**
A2 (3-30 mg/mmol)	**117 (33.5%)**
A3 (>30 mg/mmol)	**122 (35.0%)**
Total	349 (100%)

*17 patients without baseline UACR (4.6%)

Comparing with FLOW cohort?





eGFR + **UACR**

ml/min/1.73m² **mg/mmol**

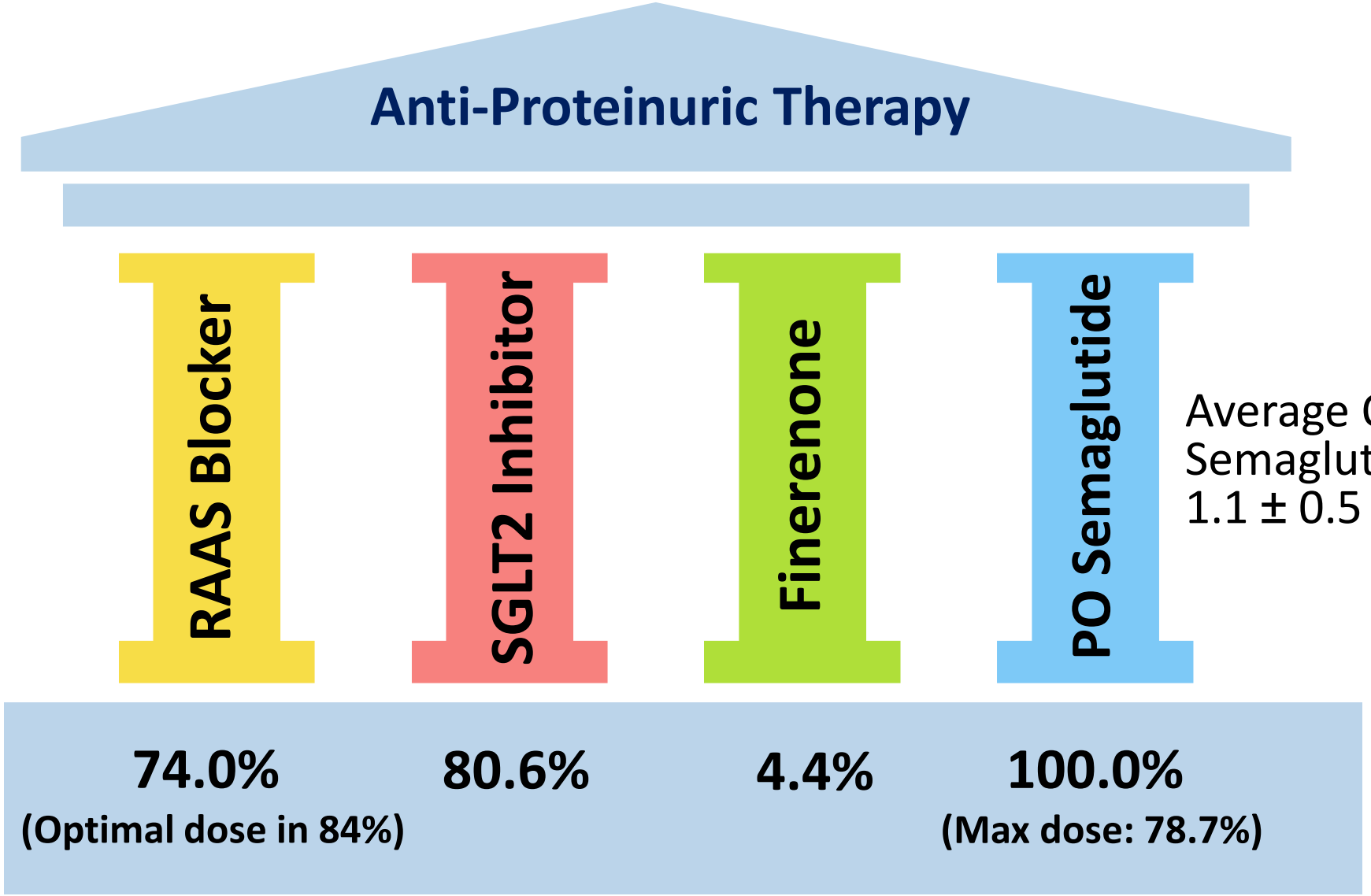
≥50 >34 (300mg/g)

<50 >11 (100mg/g)

UACR Category	N (%)
eGFR ≥50 + UACR ≥34	**43 (12.3%)**
eGFR ≥50 + UACR <34	201 (57.6%)
eGFR <50 + UACR ≥11	**88 (25.2%)**
eGFR <50 + UACR <11	17 (4.9%)
Total	349 (100%)

37.5% fulfilled FLOW inclusion criteria

Baseline Characteristics



Average Oral Semaglutide Use: 1.1 ± 0.5 years

Outcomes

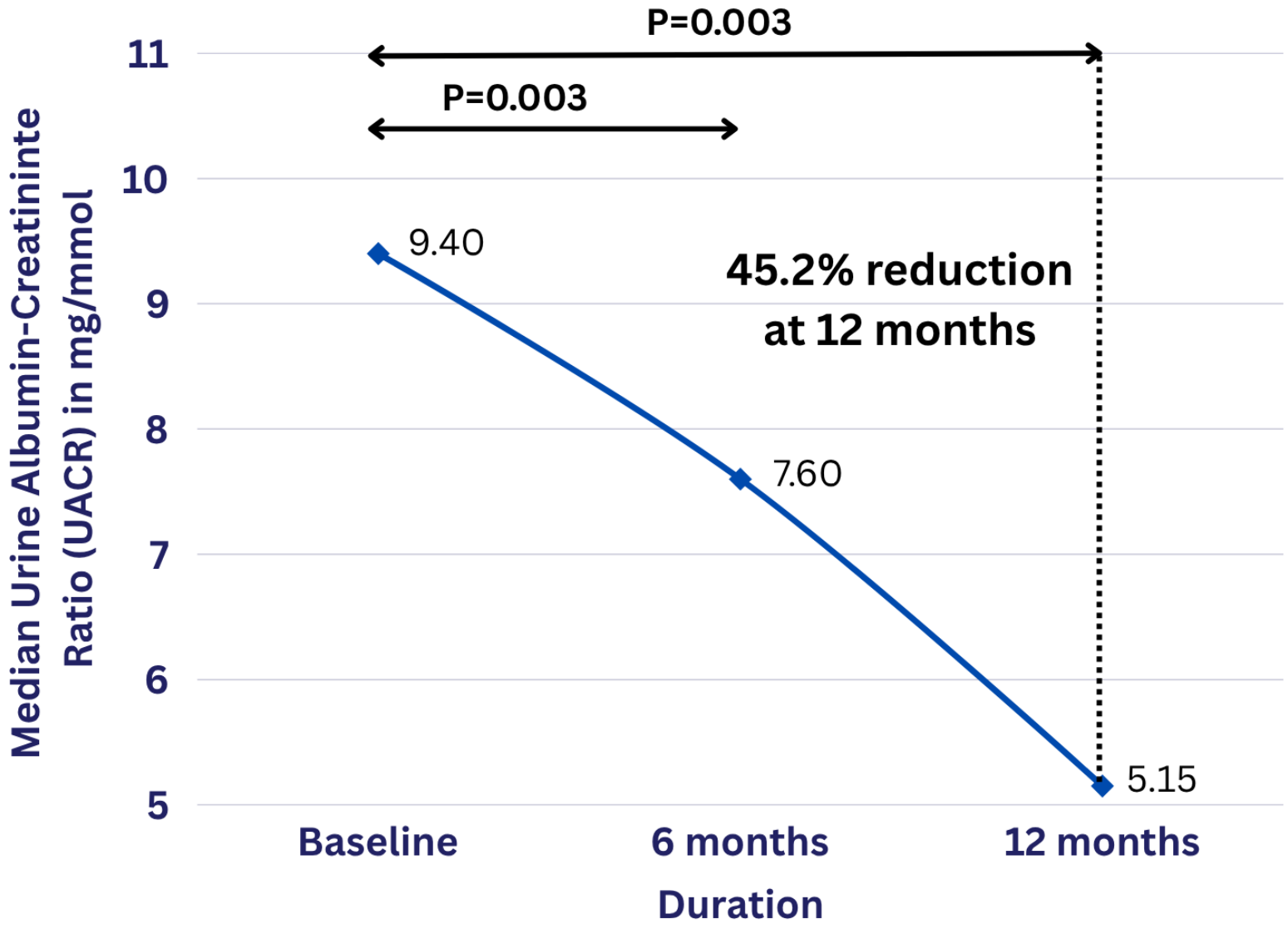
Primary

- Albuminuria (UACR) reduction
- eGFR slope

Secondary

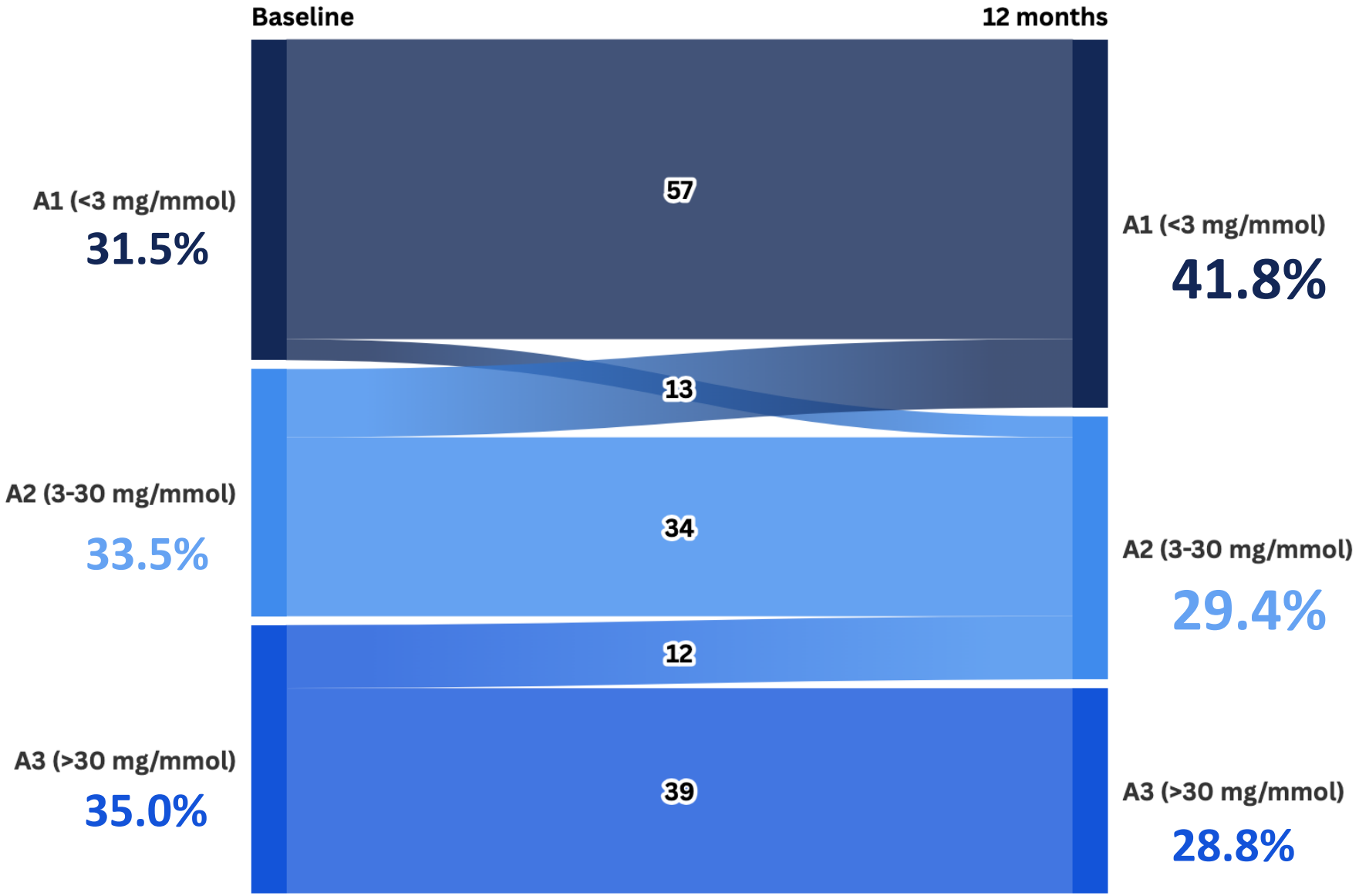
- Weight and BMI
- Blood pressure
- Metabolic profiles (HbA1c, Daily insulin requirement, Lipid profile)
- Discontinuation rate
- Safety profile (adverse event)

Albuminuria (UACR) Reduction

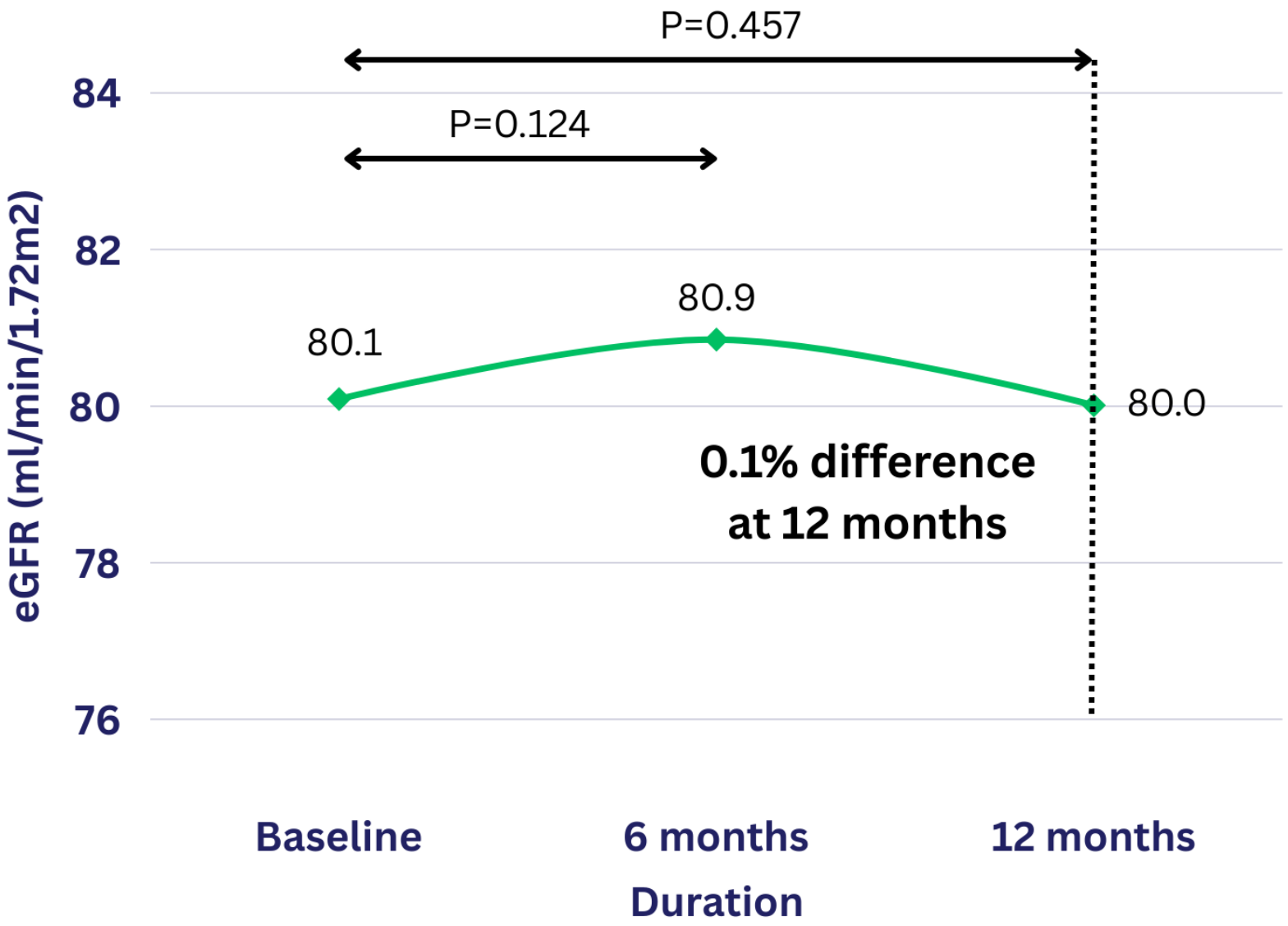


Based on Wilcoxon Signed Rank Test, adjusted by the Bonferroni correction for multiple tests

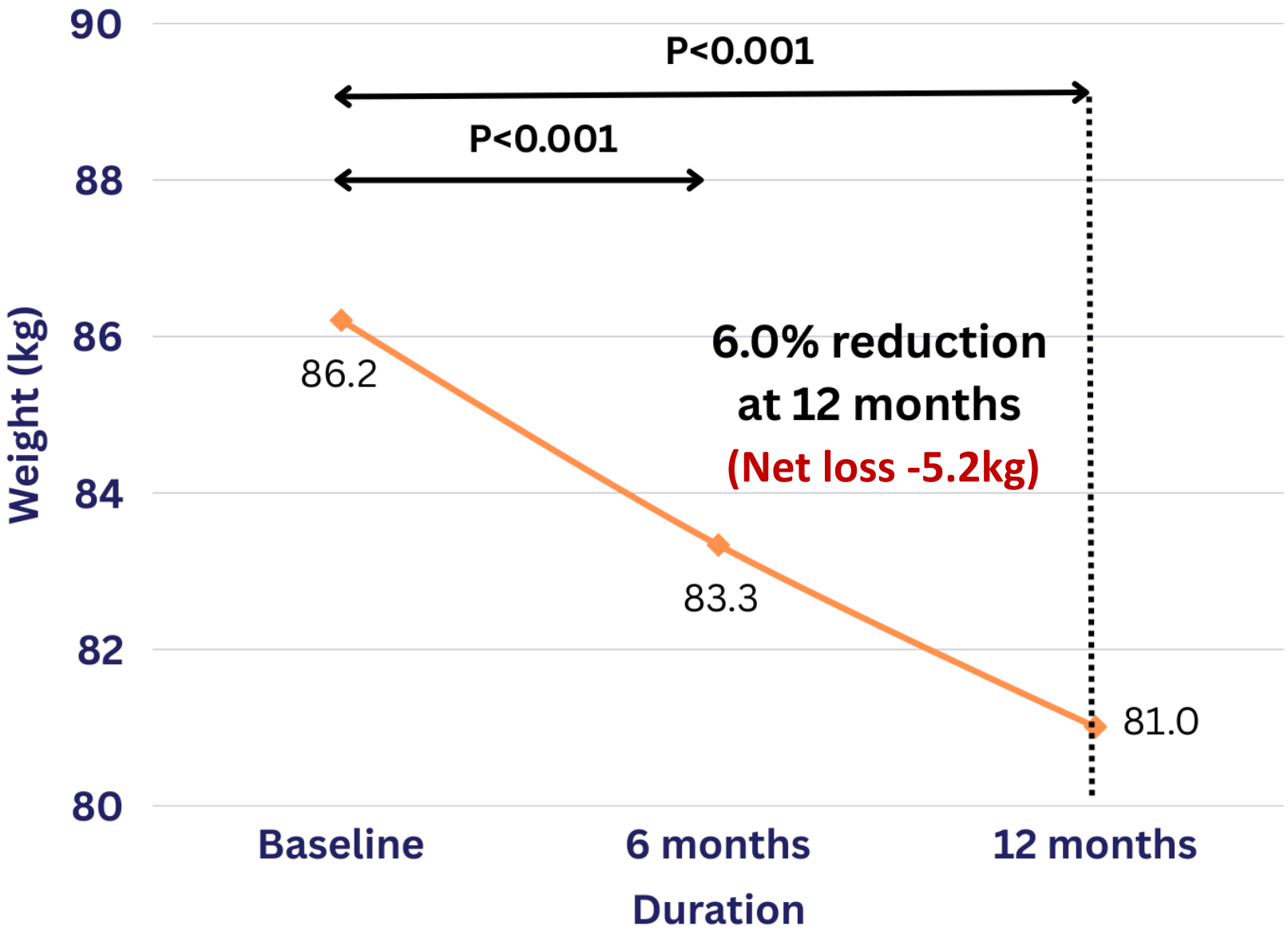
Change in Albuminuria



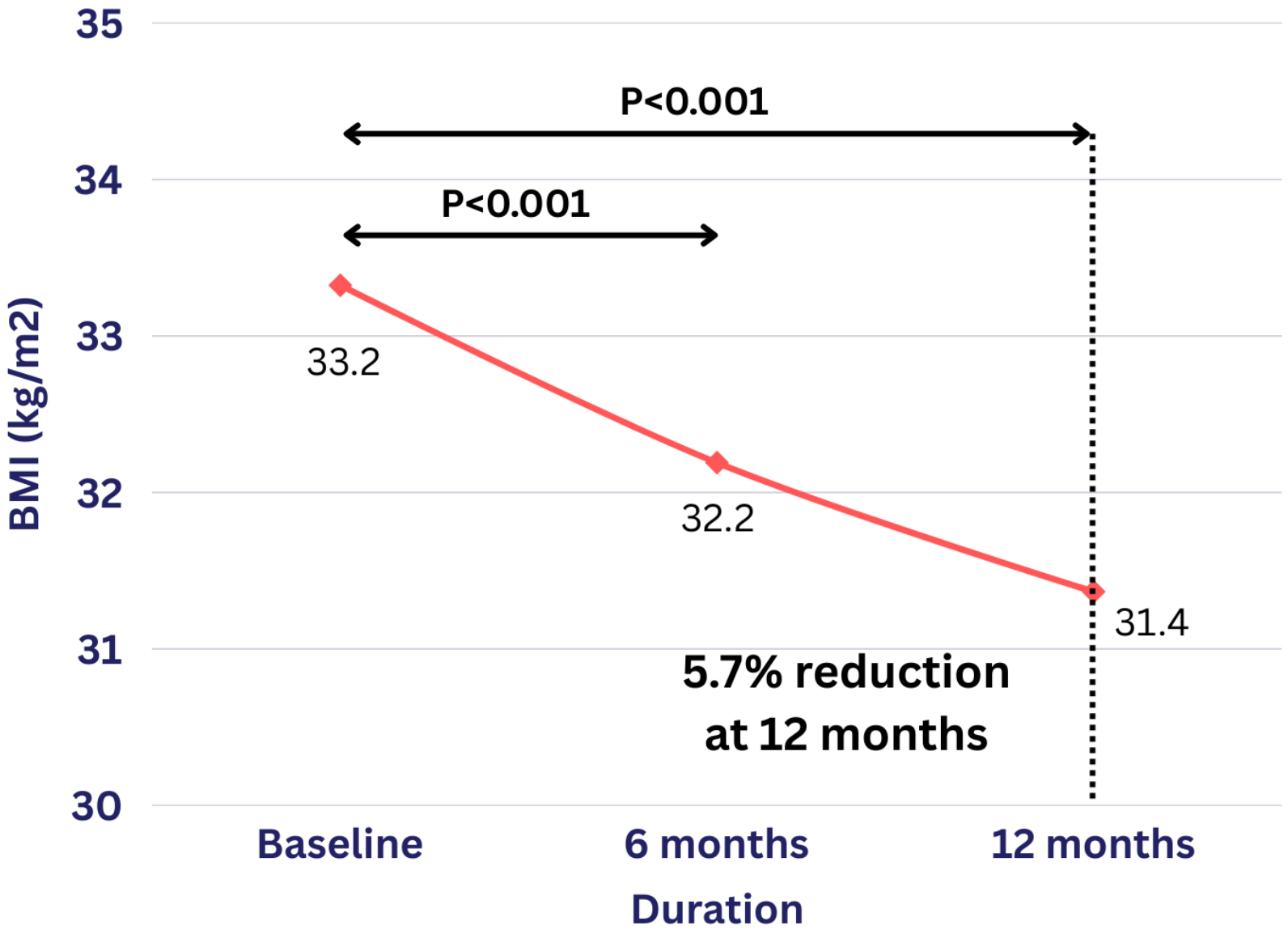
eGFR Trend


P=0.457
P=0.124
84
82
80
78
76
eGFR (ml/min/1.72m2)
80.1
80.9
80.0
0.1% difference
at 12 months
Baseline
6 months
12 months
Duration

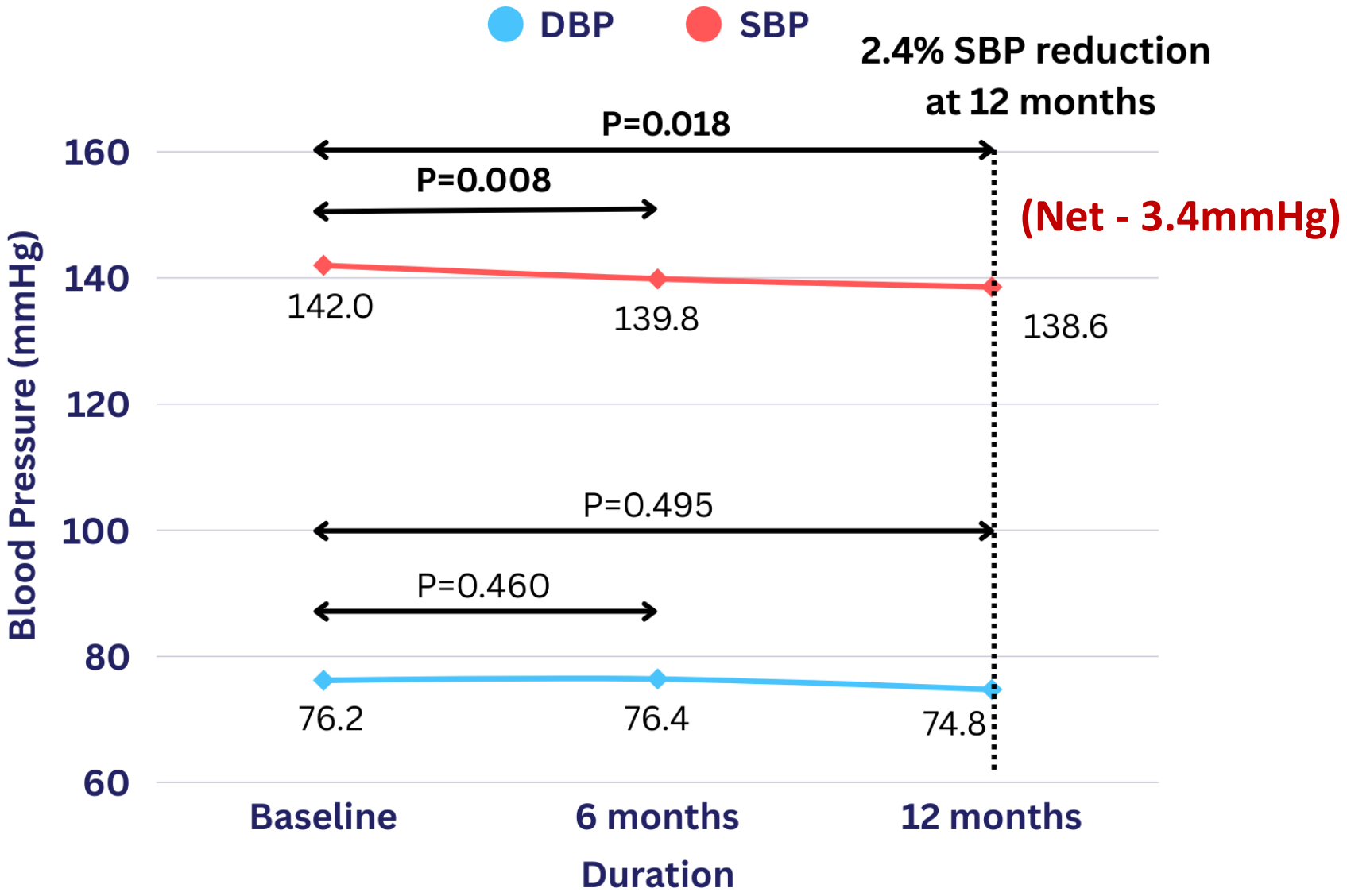
Weight Reduction



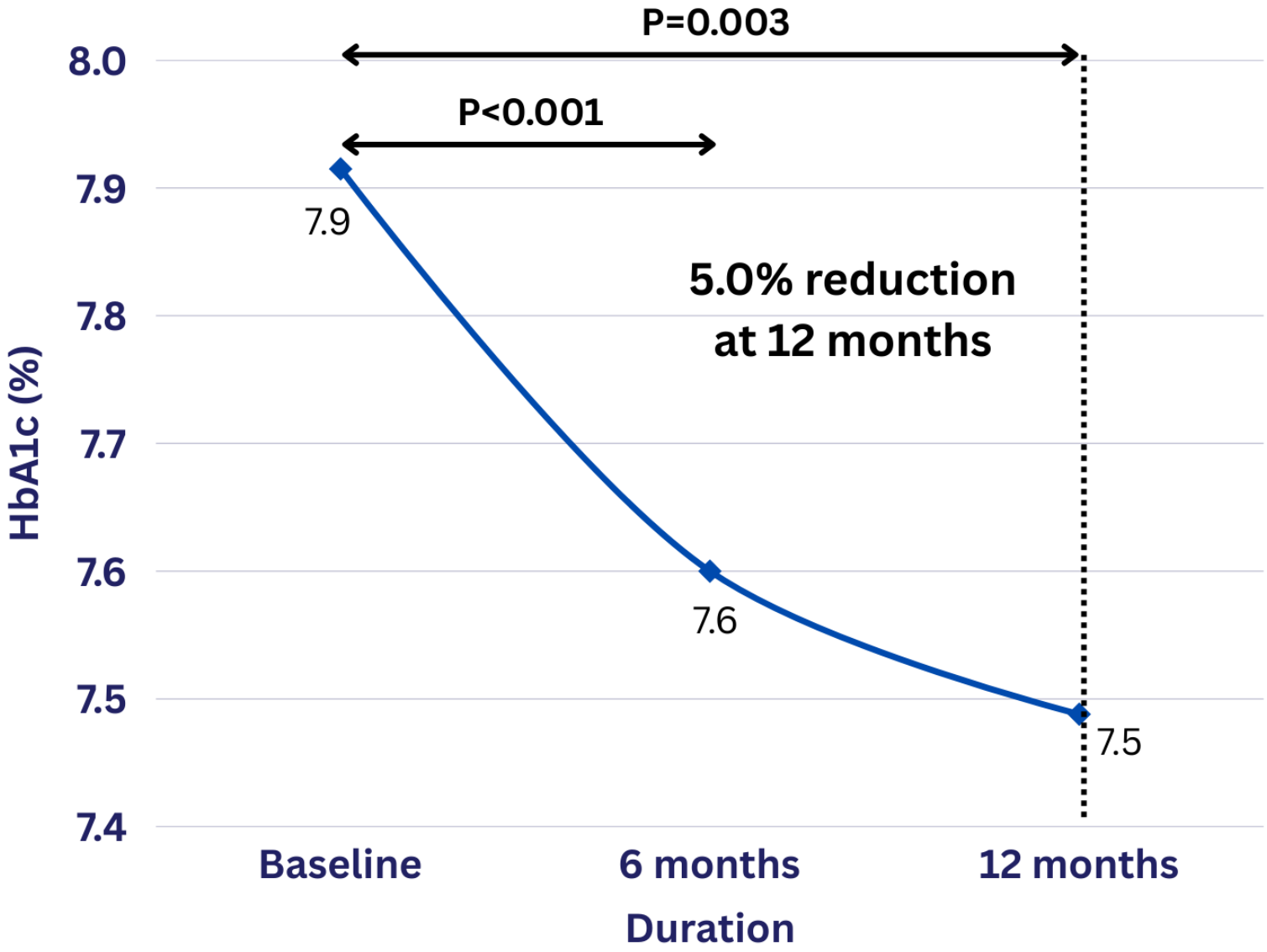
BMI Reduction



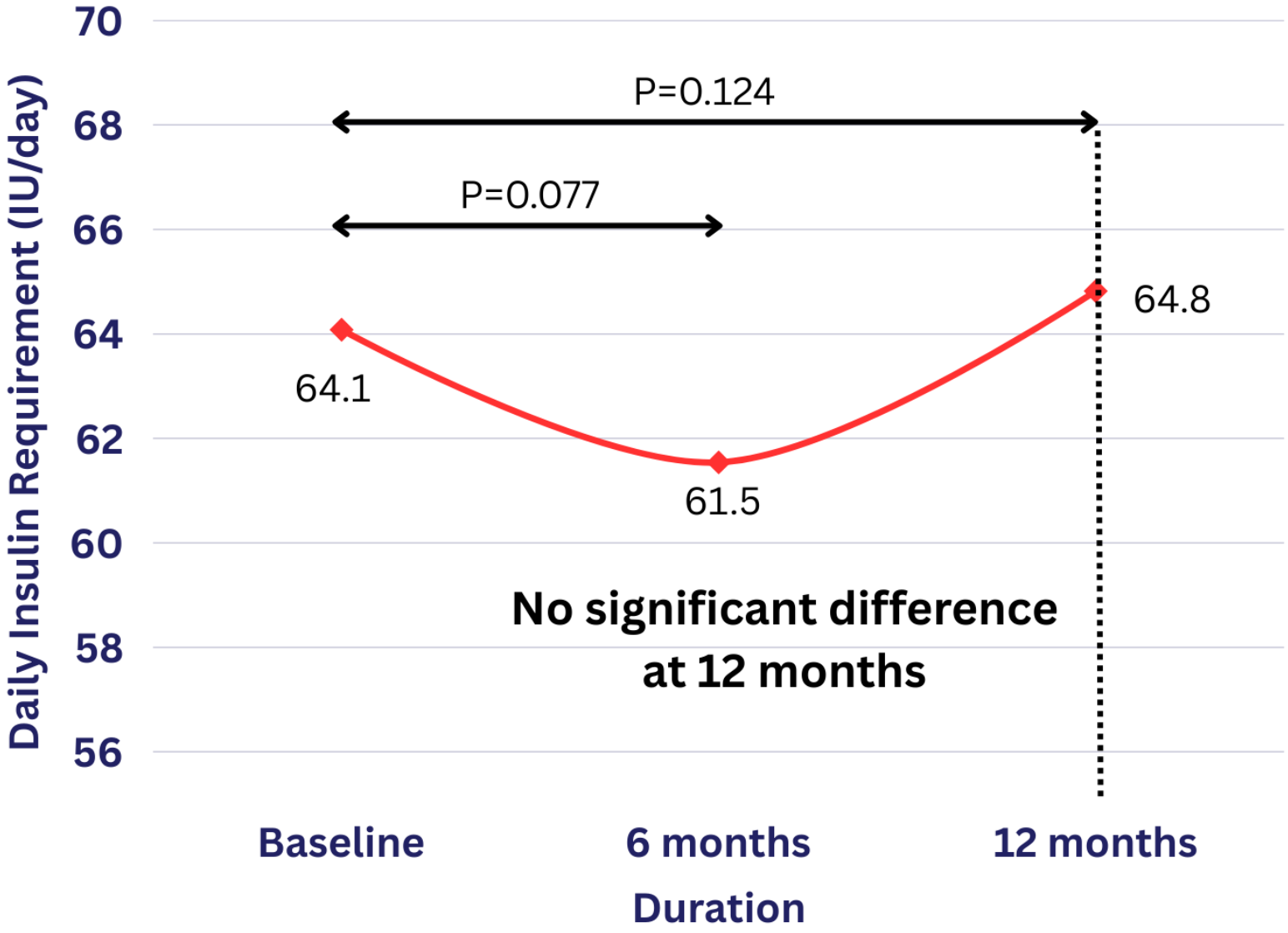
Blood Pressure Trend



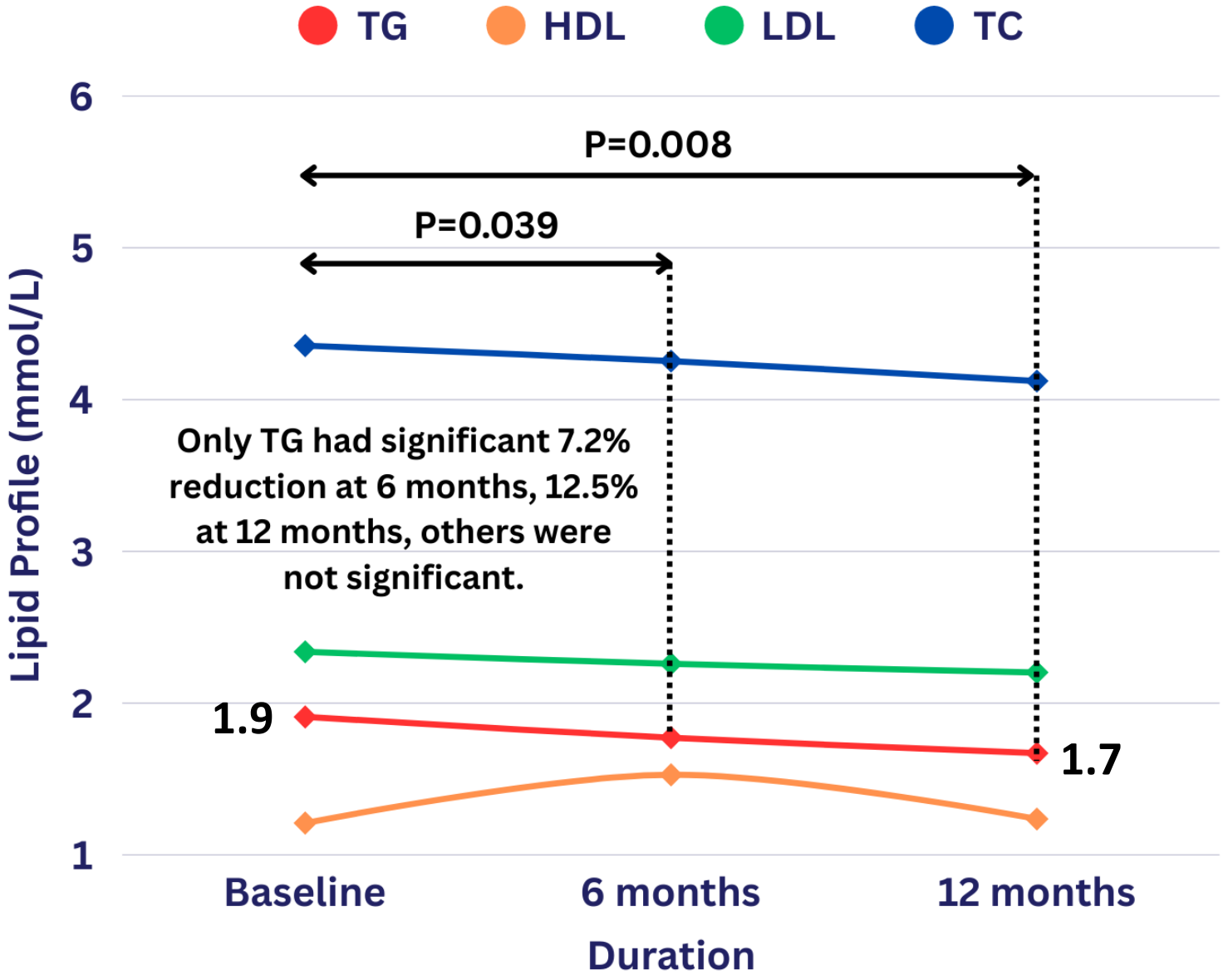
HbA1c Reduction



Daily Insulin Requirement

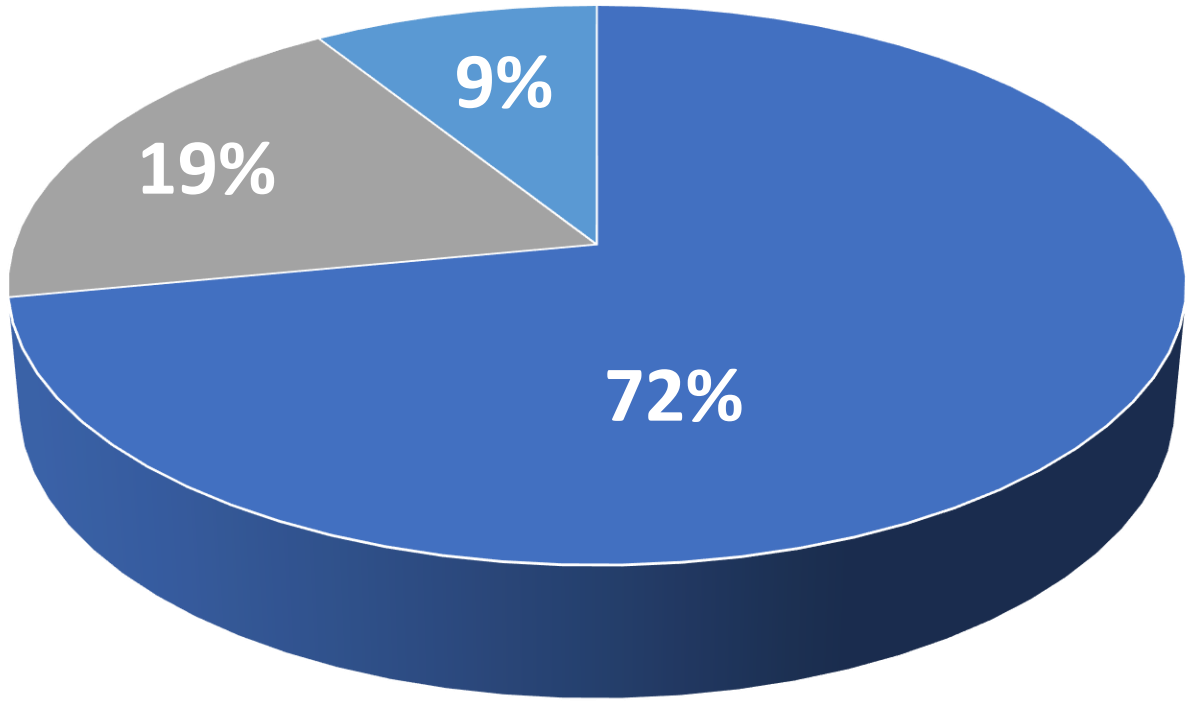


Lipid Profile Trend



Discontinuation Rate

Occurred in 54 patients (14.8%)



Gastrointestinal-related Adverse Events

Adverse Events	Percentages
Nausea/Vomiting	18.3%
Hypoglycaemia	2.2%
Diarrhoea	1.9%
Constipation	1.9%
Abdominal pain	1.4%
Heartburn	0.5%

Discussion

- Oral Semaglutide showed a significant **45.2% albuminuria reduction (p=0.003)** with eGFR stabilisation at 12 months
- Subgroup analyses (dosing):
  - At 7mg OD: 34.1% UACR reduction (p=0.034) at 12 months
  - At 14mg OD: 83.7% UACR reduction (p=0.021) at 12 months
- Overall improvements in weight/BMI, HbA1c, serum triglyceride
- Modest systolic blood pressure (SBP) changes of -3.4mmHg
- GI-related adverse events led to discontinuation: 10.7%

Strengths

- Prospective study
- Real-world evidence (reflects real-life DKD patients)
- Multi-centred
- Wide range of DKD patients (avoid selection bias)
- Provides hard primary kidney endpoints: eGFR & UACR trend
- Generalisability: representative of Malaysia population

Limitations

- Registry-based data collection
- Lack of adherence data
- Limited follow-up duration (ongoing study)
- Confounder considerations: on SGLT2i and nsMRA
- Cost/logistics consideration: may not be applicable for all healthcare facilities (accessibility and cost)

Oral **S**emaglutide Use in the Real **WO**rld, Multi-Centre Experience on **R**enal Outcomes of **D**iabetic Kidney Disease in Malaysia (**SWORD**)

SWORD TRIAL

Malaysia

366 Adults with T2DM & DKD

Female: 51.9%

Average Age: 57.5 years

Diabetes duration: ~14.8 years
48.1% male

Primary Outcomes: Significant Renal Protection at 12 Months

45.2%
Reduction in Albuminuria
Significant median reduction in UACR; direct protective effect (P=0.003)

Stabilized Kidney Function (eGFR)
eGFR trend remained stable, suggesting a halt in progression (P=0.457)

Secondary Outcomes: Widespread Metabolic Benefits

5.2 kg
Average Weight Loss
Significant mean reduction and 5.7% decrease in BMI (P<0.001)

5.0%
Reduction in HbA1c
Significant improvement in long-term blood sugar control (P=0.003)

3.4 mmHg
Reduction in Systolic Blood Pressure
Statistically significant improvement (P=0.016)

12.5%
Improvement in Triglycerides
Positive impact on serum triglyceride levels (P=0.008)

23.5%

Pre-existing Cardiovascular Disease

- RAAS blockade (74%)
- SGLT-2 inhibitors (80.6%)
- nsMRA: Finerenone (4.4%)

Nearly 400 days

Average Treatment Duration
Mean use: 386.8 days (78.7% on 14mg dose)

Safety & Tolerability Profile

Favorable Safety Profile
Well tolerated with minimal side effects reported by majority

18.3%
Experienced Nausea or Vomiting
Most common side effect (hypoglycemia 2.2%, diarrhea 1.9% were rare)

14.8%
Discontinued Treatment
Of those who stopped, 72.2% due to gastrointestinal side effects

JM Em, SK Lim et al. APCN x TSN 2025

Filling the Gaps in the Current Evidences of GLP-1RA based Therapies

	SC Liraglutide (Saxenda)	SC Semaglutide (Ozempic/Wegovy)	PO Semaglutide (Rybelsus)	SC Tirzepatide (Mounjaro)
T2DM	LEAD (DM)	SUSTAIN 1-7 (DM)	PIONEER-6 (DM)	SURPASS (DM)
Overweight/Obese	SCALE (non-DM)	STEP-1 (non-DM)	OASIS-1 (non-DM)	SURMOUNT (non-DM)
CKD		FLOW (DM) SMART (non-DM)	ENDO2S-RWD (DM) SWORD (DM)	TREASURE-CKD (DM, non-DM)
CVOT	LEADER (DM)	SUSTAIN-6 (DM) SELECT (non-DM)	SOUL (DM)	SURPASS-CVOT SURMOUNT-MNO
HFpEF		STEP-HFpEF (non-DM) STEP-HFpEF-DM (DM)		SUMMIT (Non-DM)
MAFLD/MASH	LEAN	ESSENCE		SYNERGY-NASH
OSA	SCALE-SA			SURMOUNT-OSA
PVD	STARDUST (DM)	STRIDE (DM)		
Cognition (AD)	ELAD		EVOKE/EVOKE+	

AD: Alzheimer's Disease; CVOT: Cardiovascular Outcome Trial; MAFLD: Metabolic Associated Fatty Liver Disease; MASH: Metabolic Associated Steatohepatitis; HFpEF: Heart Failure with Preserve Ejection Fraction; OSA: Obstructive Sleep Apnoea; PVD: Peripheral Vascular Disease

Thank you.