



Hyperkalemia Management in Older Adults With Diabetic Kidney Disease Receiving Renin-Angiotensin-Aldosterone System Inhibitors: A Post Hoc Analysis of the AMETHYST-DN Clinical Trial

George L. Bakris, Steven D. Woods, Paula J. Alvarez, Susan P. Arthur, and Rajeev Kumar

Rationale & Objective: Older people are more likely to have reduced kidney function and multiple comorbid conditions predisposing them to hyperkalemia. This post hoc subgroup analysis aimed to evaluate the effectiveness of patiromer, a sodium-free nonabsorbed polymer, in lowering serum potassium levels in older patients receiving a renin-angiotensin-aldosterone system inhibitor with chronic kidney disease (CKD), type 2 diabetes mellitus (T2DM), and hypertension.

Study Design: Post hoc subgroup analysis of the randomized open-label AMETHYST-DN clinical trial.

Setting & Participants: Multicenter clinical trial. Individuals 75 years and older with CKD, T2DM, hypertension, and hyperkalemia at baseline (N = 60; mean age, 77 years; 30 men [50%]; mean estimated glomerular filtration rate, 41.6 ± 14.3 mL/min/1.73 m²).

Intervention: Patients with hyperkalemia were randomly assigned to receive patiromer at doses ranging from 4.2 to 16.8 g twice daily.

Outcomes: We evaluated changes in serum potassium levels from baseline to week 4 and time points through 52 weeks. Long-term safety and tolerability were assessed through the end of

52 weeks and included frequency of adverse events, clinical laboratory measurements, and vital signs.

Results: Of 306 AMETHYST-DN participants, 60 were 75 years or older. All 60 patients had CKD and T2DM; 37% had heart failure. At screening, patients had an estimated glomerular filtration rate of 42 mL/min/1.73 m², median urinary albumin-creatinine ratio of 127 mg/g, and baseline mean serum potassium level of 5.19 mEq/L. Mean serum potassium level was reduced at each time point from the first postbaseline visit (day 3) through week 52.

Limitations: This small subgroup analysis was not prespecified and therefore randomization was lost; thus, it should be considered hypothesis generating.

Conclusions: Among older patients with hyperkalemia and diabetic kidney disease, treatment with patiromer resulted in significant reductions in serum potassium levels after 4 weeks and lasted through 52 weeks. Patiromer was effective in lowering serum potassium levels and was well tolerated in older patients.

Funding: Vifor Pharma, Inc.

Trial Registration: NCT01371747

Visual Abstract included

Complete author and article information provided before references.

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Kidney Med. 3(3):360-367. Published online March 13, 2021.

doi: 10.1016/j.xkme.2021.01.005

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People older than 65 years have increased susceptibility to developing hyperkalemia, with resultant poor outcomes.^{1,2} This is due to multiple comorbid conditions, such as chronic kidney disease (CKD), cardiovascular disease/heart failure, and type 2 diabetes mellitus. Patients with high risk for developing hyperkalemia are those taking a renin-angiotensin-aldosterone system (RAAS) inhibitor to treat kidney disease and heart failure.^{3,4} Regardless of age, guideline-recommended doses of RAAS inhibitor medications are indicated to slow the progression of diabetic kidney disease, but the inherent risk for developing hyperkalemia precludes their use in a subset of patients.^{3,5,6} Hence, RAAS inhibitor use is either downtitrated or discontinued.^{4,5,7}

Patiromer is a calcium-based nonabsorbed polymer that binds potassium in the gastrointestinal tract and is approved in the United States and European Union for the treatment of hyperkalemia.^{8,9} Long-term daily ingestion of patiromer is safe, well-tolerated, and effective at lowering

serum potassium levels in both short- and long-term clinical trials.^{10,11} In the previously published AMETHYST-DN trial, while receiving patiromer, patients with diabetic kidney disease and hypertension observed significantly decreased mean serum potassium levels through 4 weeks and consistently maintained normal levels over 52 weeks.¹¹

We report the results of a post hoc subgroup analysis of the AMETHYST-DN trial¹¹ (ClinicalTrials.gov identifier: NCT01371747) to determine the efficacy and safety of patiromer for the treatment of hyperkalemia in patients 75 years and older.

METHODS

Study Design and Patient Population

The protocol of the AMETHYST-DN trial was approved by local or national independent ethics committees at each study site and performed in accordance with the

PLAIN-LANGUAGE SUMMARY

Hyperkalemia is a common electrolyte abnormality in patients with chronic kidney disease, diabetes, and/or heart failure. Due to underlying conditions and use of multiple medications, older patients are particularly predisposed to develop this electrolyte disturbance. In this post hoc subgroup analysis, we evaluated change in serum potassium levels in patients 75 years and older who received patiromer over a 52-week period. Sixty patients were included, and mean serum potassium level was reduced at each time point following the first baseline visit. Patiromer was well tolerated and effectively lowered serum potassium levels in this older population of patients with diabetes and kidney disease.

International Conference on Harmonization E6 Guideline for Good Clinical Practice, the Declaration of Helsinki principles, and local or national independent ethics committee requirements. All patients provided written informed consent before any study-specific procedures were performed.

The design of the AMETHYST-DN trial has been described previously as a multicenter open-label dose-ranging trial of 306 randomly assigned patients aged 30 to 80 years with CKD (estimated glomerular filtration rate [eGFR], 15 to <60 mL/min/1.73 m²), type 2 diabetes mellitus, and hypertension.¹¹ Patients with hyperkalemia

(potassium > 5.0 to <6.0 mEq/L) at screening or after an up to 4-week run-in period were randomly assigned. All patients had been receiving a stable dose of RAAS inhibitor for 28 days or longer before screening.

The 52-week study included an 8-week treatment period and 44-week long-term maintenance period for up to 52 weeks of total treatment and posttreatment follow-up of 4 weeks (Fig 1). Patients who were normokalemic (potassium, 4.3–5.0 mEq/L) at screening entered a run-in period (up to 4 weeks) and either switched from their current angiotensin-converting enzyme (ACE) inhibitor or angiotensin receptor blocker (ARB) medication to a maximum labeled dose of ARB (100 mg/d of losartan) and/or up to 50 mg of spironolactone (cohort 1) or continued their current ACE inhibitor or ARB treatment and added up to 50 mg of spironolactone (cohort 2). Patients who developed hyperkalemia at any point during the 4-week run-in period could be randomly assigned into the treatment phase. Patients with preexisting hyperkalemia (potassium >5.0 to <6.0 mEq/L) at screening (cohort 3) continued use of their prescribed ACE inhibitor or ARB, skipped the run-in period, and were randomly assigned directly to the treatment phase.

Patients entering the treatment period were stratified to 1 of 2 strata: mild (serum potassium >5.0 to 5.5 mEq/L) and moderate hyperkalemia (serum potassium >5.5 to <6.0 mEq/L). These patients were randomly assigned to 1 of 3 starting doses of patiromer per stratum: patients with mild hyperkalemia received 4.2, 8.4, or 12.6 g twice

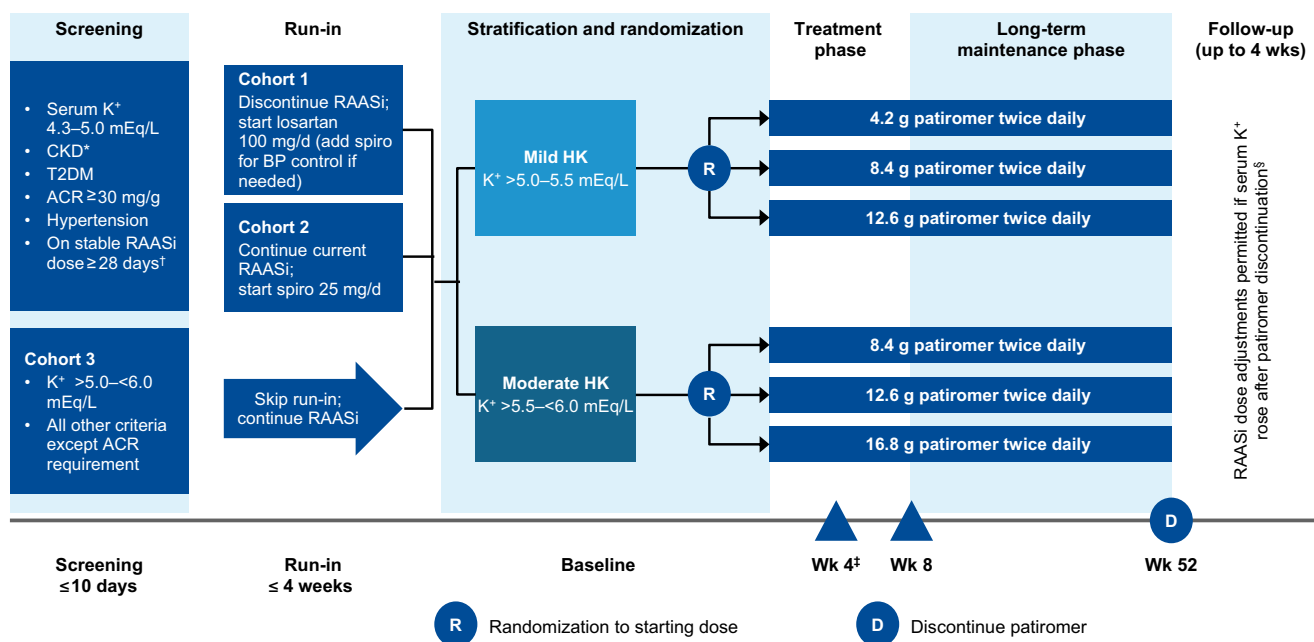


Figure 1. AMETHYST-DN study design. *Estimated glomerular filtration rate (eGFR) of 15 to <60 mL/min/1.73 m². [†]Before screening. [‡]Primary end points. [§]Renin-angiotensin-aldosterone system inhibitor (RAASi) therapy was continued after patiromer treatment discontinuation only in patients who were normokalemic (mean serum potassium ≤ 5.0 mEq/L) at the end of the maintenance phase. Abbreviations: ACR, albumin-creatinine ratio; BP, blood pressure; CKD, chronic kidney disease; HK, hyperkalemia; spiro, spironolactone; T2DM, type 2 diabetes mellitus.

Table 1. Baseline Demographics

Patient Characteristics	Patients Aged ≥75 Years With CKD and T2DM (N = 60)
Age, y	77 ± 1.45
Male sex	30 (50%)
White race	60 (100%)
eGFR at screening, mL/min/1.73 m ²	41.6 ± 14.3
Urinary ACR, mg/g	127 (3, 6,942)
Heart failure (NYHA I/II)	22 (37%)
Drugs used for diabetes	60 (100%)
RAAS inhibitor medications	
ACE inhibitor	36 (60%)
ARB	10 (17%)
Aldosterone antagonist	1 (1.6%)
RAASi combination ^a	13 (27%)
Any single RAAS inhibitor	54 (90%)
β-Blocker	28 (47%)
Non-RAASi diuretic	26 (43%)
Cohort 1	12 (20%)
Cohort 2	0 (0%)
Cohort 3	48 (80%)

Values expressed as mean ± standard deviation, number (percent), and median (minimum, maximum).

Abbreviations: ACEI, angiotensin-converting enzyme inhibitor; ACR, albumin-creatinine ratio; ARB, angiotensin receptor blocker; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; NYHA, New York Heart Association; RAASi, renin-angiotensin-aldosterone system inhibitor; T2DM, type 2 diabetes mellitus.

^aRAASi combination: RAASi medication combined with a non-RAASi medication.

daily and patients with moderate hyperkalemia received 8.4, 12.6, or 16.8 g twice daily. Following the baseline visit, patients were assessed at day 3, weekly thereafter during the 8-week treatment period, and monthly during the 44-week long-term maintenance period. The starting dose could be titrated up or down to achieve and maintain serum potassium levels ≤5.0 mEq/L during the treatment and long-term maintenance periods. By protocol, the RAAS inhibitor dose could not be dwnitratred or discontinued because of hyperkalemia, but patiromer could be uptitrated using a protocol-defined dosing algorithm.

At the end of the long-term maintenance period, all patients with serum potassium levels >5.0 mEq/L discontinued patiromer treatment and all RAAS inhibitor medications and were followed up for 2 visits within 7 days. Patients with serum potassium level ≤5.0 mEq/L (normokalemic) at the end of the long-term maintenance period discontinued patiromer treatment but remained receiving RAAS inhibitors for 28 days and returned for 5 follow-up visits (day 3 and weekly through week 4 posttreatment).¹¹

In this post hoc subgroup analysis, all 3 starting dose groups within each stratum (mild or moderate) were combined to evaluate the effect of patiromer on serum potassium levels.

Efficacy and Safety Assessments

In this post hoc subgroup analysis of patients 75 years and older, we analyzed a selection of the same end points as in the AMETHYST-DN study.¹¹ We evaluated change in serum potassium levels from baseline to week 4 and changes in serum potassium levels at multiple time points over time. All assessments of serum potassium values were based on central laboratory measurements.

Long-term safety and tolerability were assessed through the end of the long-term maintenance period at 52 weeks and included frequency of adverse events, clinical laboratory measurements, and vital signs.

Statistical Analysis

Details of the statistical analysis of the AMETHYST-DN trial have been described previously.¹¹ For this post hoc subgroup analysis, mean decreases in serum potassium levels at weeks 4 and 52 were estimated using analysis of covariance models with baseline serum potassium level (local serum potassium >5.0 to 5.5 or >5.5 to <6.0 mEq/L) as a fixed effect and baseline serum potassium level as a continuous covariate. All statistical analyses were performed using SAS, version 9.4 (SAS Institute Inc).

RESULTS

Patient Disposition

Of the 306 patients who were randomly assigned to treatment in the AMETHYST-DN study, 60 patients aged 75 years and older were assessed by investigators (cohort 1 [n = 12] and cohort 3 [n = 48]). Disposition is shown in Fig S1. All 60 patients were treated with at least 1 dose of patiromer and were included in the safety and efficacy analyses. Mean age of this subgroup population was 77 years, all patients were White, and half were men. Mean eGFR at screening was 42 mL/min/1.73 m² (Table 1). All 60 patients had hypertension and type 2 diabetes mellitus. At baseline, mean serum potassium level was 5.19 mEq/L; 49 patients (82%) had a serum potassium between >5.0 and 5.5 mEq/L (mild hyperkalemia), and 11 (18%) had a serum potassium level > 5.5 to <6.0 mEq/L (moderate hyperkalemia). Of the 60 patients randomly assigned, 53 (88.3%) completed the treatment period, 47 (78.3%) entered the long-term maintenance period, and 40 (66.7%) completed the entire study. The most common reasons for early withdrawal during the entire study were consent withdrawal (n = 6), adverse events (n = 5), and nonadherence (n = 4; Fig S1). Ten of 12 patients from cohort 1 completed the treatment phase, receiving the optimal dose of losartan of 100 mg/d. Of these, 10 patients entered the long-term maintenance period, with 9 (90%) completing the full 52 weeks.

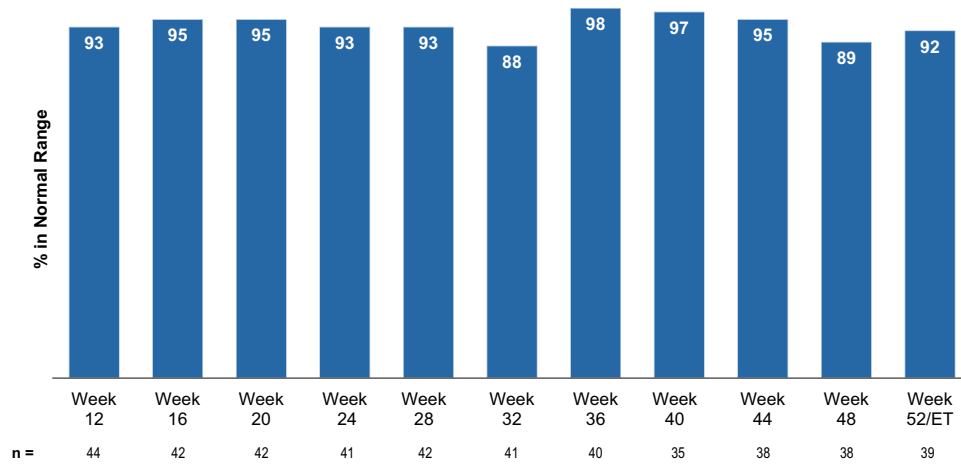


Figure 2. Achievement of normokalemia. Abbreviation: ET, end of treatment.

Efficacy

Mean serum potassium level was reduced at each time point from the first postbaseline visit (day 3) through week 52. At week 4, a significant reduction in least squares mean change from baseline was observed (−0.65 mEq/L; $P < 0.001$). At week 52 (end of treatment), the observed least squares mean reduction was −0.61 mEq/L ($P < 0.001$). Most patients entering the long-term maintenance period had serum potassium levels in the target or normal range (3.8–5.0 mEq/L). At each time point of the maintenance phase, between 88% and 98% of patients were observed to have serum potassium levels in the normal range (Fig 2). At week 52 (end of treatment), all 60 patients (100%) had serum potassium levels <5.5 mEq/L, and 95% had serum potassium levels <5.0 mEq/L. These findings correlate with the original AMETHYST-DN investigation, with reductions in serum potassium levels at all time points to week 52.

Upon discontinuation of patiomer treatment at 52 weeks, similar to the original investigation, an increase in mean serum potassium level was observed (Fig 3). After 3, 7, and 14 days of patiomer treatment discontinuation, mean serum potassium levels were 4.79, 4.85, and 4.95 mEq/L, respectively. This increase in mean serum potassium level during the follow-up period plateaued at 21 and 28 days of cessation. This plateau is most likely due to protocol-required discontinuation of RAAS inhibitor medications in patients with serum potassium levels >5.0 mEq/L.

Safety

Patiomer was generally well tolerated in this older adult subgroup of patients (Table 2). Over 52 weeks, 31 (52%) patients reported at least 1 treatment-emergent adverse event, with 10 patients (17%) reporting at least 1 adverse

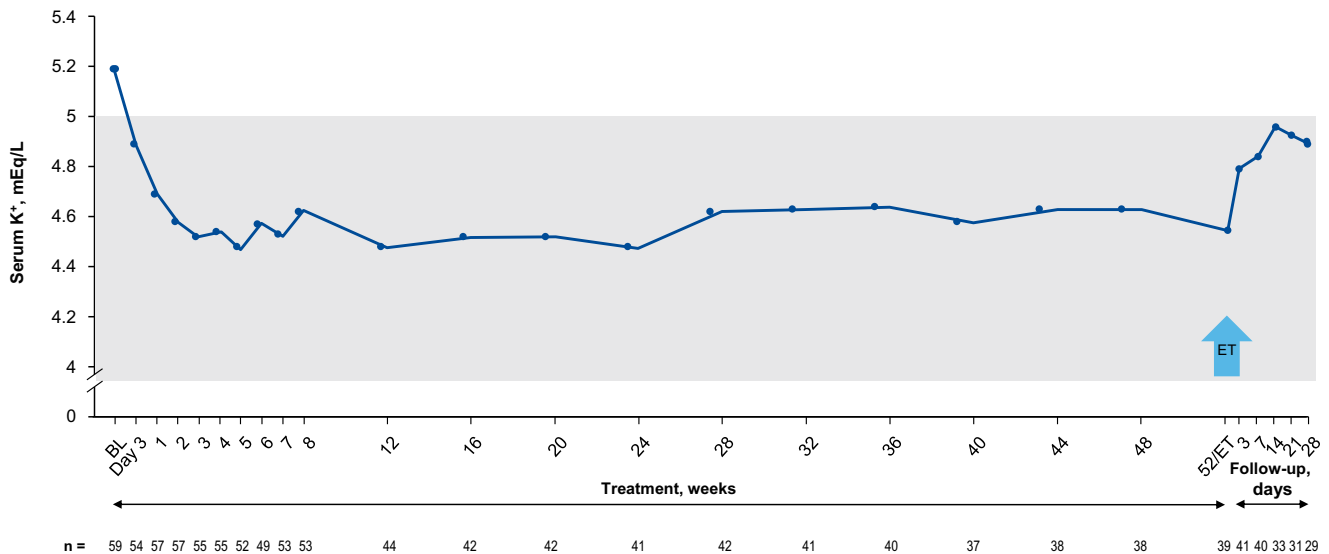


Figure 3. Mean serum potassium level at each time point. Abbreviations: BL, baseline; ET, end of treatment.

Table 2. Treatment-Related Adverse Events Related to Patiromer With Onset Over the Entire Treatment Period

Treatment-Related Adverse Event	Patients Aged ≥ 75 y (N = 60)
Hypomagnesemia ^a	4 (6.6%)
Atrial flutter	2 (3.3%)
Constipation	2 (3.3%)
Abdominal discomfort	1 (1.7%)
Gastroesophageal reflux disease	1 (1.7%)
Vomiting	1 (1.7%)

Values expressed as number (percent).

^aOne patient receiving 8.4 g/d, 1 patient receiving 16.8 g/d, and 2 patients receiving 25.2 g/d. Other treatment-emergent adverse event investigation: blood magnesium levels decreased in 1 patient (receiving 25.2 g/d).

event considered related to patiromer by the investigator; none were considered serious. The most frequently identified treatment-emergent adverse event ($\geq 5.0\%$ of patients, regardless of stratum or dose) was hypomagnesemia (6.6%). No patients discontinued treatment due to hypomagnesemia, and there was no case of severe hypomagnesemia (magnesium < 1.0 mg/dL) or hypokalemia (potassium < 3.5 mEq/L). Constipation was reported in 2 patients (3.3%), and both cases were considered mild to moderate. Six patients (10%) reported at least 1 adverse event leading to patiromer treatment discontinuation. The most common adverse events leading to patiromer treatment discontinuation were gastrointestinal disorders (constipation and vomiting) in 2 patients and chronic kidney failure, also in 2 patients.

Mean serum calcium and magnesium levels remained in the normal range through 52 weeks of the trial regardless of the stratum. At week 4, mean serum calcium change increased slightly from baseline in the mild hyperkalemia group (0.12 mg/dL) and decreased slightly in the moderate hyperkalemia group (-0.05 mg/dL). At 52 weeks, there was no change observed from baseline in mean serum calcium level in the mild hyperkalemia group and a slight increase of 0.28 mg/dL in the moderate hyperkalemia group, with patients receiving patiromer 25.2 and 33.6 g/d, respectively. Mean serum magnesium level decreased slightly at 4 weeks and remained stable through 52 weeks (end of treatment; Table 3). The week 4 serum magnesium mean changes from baseline were -0.09 mg/dL in the mild hyperkalemia groups and -0.13 mg/dL in the moderate hyperkalemia groups. At 52 weeks (end of treatment), serum magnesium level changes from baseline were -0.06 mg/dL and -0.08 mg/dL, respectively. There was no clinically meaningful reduction in mean eGFR and mean urinary albumin-creatinine ratio during the study.

DISCUSSION

The results of this post hoc analysis confirm that patiromer is effective in lowering and maintaining serum potassium levels over the long term in a safe range in previously hyperkalemic patients 75 years and older with diabetic kidney disease receiving an RAAS inhibitor. The significant reductions in mean serum potassium levels in this older adult population at week 4 (primary end point) were consistent with the

Table 3. Serum Calcium and Magnesium Over 52 Weeks

	Serum Calcium, mg/dL		Serum Magnesium, mg/dL	
	Mild Hyperkalemia (K ⁺ > 5.0 to ≤ 5.5 mEq/L)	Moderate Hyperkalemia (K ⁺ > 5.5 to < 6.0 mEq/L)	Mild Hyperkalemia (K ⁺ > 5.0 to ≤ 5.5 mEq/L)	Moderate Hyperkalemia (K ⁺ > 5.5 to < 6.0 mEq/L)
Baseline	9.41 \pm 0.6 ^a	9.13 \pm 0.6 ^b	1.96 \pm 0.2 ^a	2.09 \pm 0.3 ^b
Week 4	9.52 \pm 0.5 ^c	9.0 \pm 0.4 ^d	1.87 \pm 0.3 ^c	1.94 \pm 0.1 ^d
Change from baseline	0.12 \pm 0.6	-0.05 \pm 0.4	-0.09 \pm 0.2	-0.13 \pm 0.2
Week 24	9.48 \pm 0.5 ^e	9.38 \pm 0.6 ^f	1.9 \pm 0.3 ^e	2.09 \pm 0.2 ^f
Change from baseline	-0.01 \pm 0.5	0.3 \pm 0.5	-0.05 \pm 0.3	0.04 \pm 0.3
Week 52/end of treatment	9.48 \pm 0.5 ^g	9.5 \pm 0.2 ^f	1.88 \pm 0.2 ^g	1.94 \pm 0.1 ^f
Change from baseline	0.0 \pm 0.6	0.28 \pm 0.4	-0.06 \pm 0.3	-0.08 \pm 0.2
Follow-up +28 d	9.5 \pm 0.6 ^h	9.4 \pm 0.4 ⁱ	1.91 \pm 0.3 ^h	2.12 \pm 0.2 ⁱ
Change from baseline	0.06 \pm 0.7	0.15 \pm 0.4	-0.04 \pm 0.3	0.12 \pm 0.1

Values expressed as mean \pm standard deviation.

^an = 49.

^bn = 10.

^cn = 46.

^dn = 9.

^en = 36.

^fn = 5.

^gn = 34.

^hn = 25.

ⁱn = 4.

previously published results observed in the overall population.¹¹ As in the previous results, patiomer consistently maintained mean serum potassium levels in the normal range for up to 1 year with very few dose titrations required and the continued maintenance of RAAS inhibitor medications in most patients. In this subgroup of older patients, 12 were randomly assigned to cohort 1 and received the targeted dose of losartan, 100 mg/d, with or without spironolactone. Ten patients completed the treatment phases, with 90% (n = 9) maintained on the guideline-recommended dose through 52 weeks.

This is the first long-term safety analysis of patiomer in patients 75 years and older. Patiomer was generally well tolerated, and its long-term safety was similar to the overall patient population.^{10,11} Overall, most discontinuations due to adverse events were not patiomer related. No episodes of serum potassium level <3.5 mEq/L or serum magnesium level <1.0 mg/dL were observed over the 1 year. Mean serum calcium levels remained in the normal range during the study, with slight increases observed at 52 weeks (0.07-0.37 mg/dL).

In the OPAL HK study, a similar post hoc subgroup analysis of patients with hyperkalemia 75 years and older on a stable dose of RAAS inhibitor therapy was conducted.⁵ This was a multicenter single-blind randomized study with 2 phases: a 4-week single-group initial treatment phase and an 8-week placebo-controlled withdrawal phase. Treatment with patiomer resulted in a mean (standard error) decrease in serum potassium level of -0.99 mEq/L from baseline to 4 weeks of the treatment phase. Patients continuing on patiomer treatment for an additional 4 weeks in the randomized withdrawal phase observed a median change in serum potassium level of -0.10 (interquartile range, -0.3 to 0.3) mEq/L, whereas for patients switched to placebo, median change was 0.60 (interquartile range, 0.40-1.10) mEq/L. The difference between treatment groups in median change was 0.70 (95% CI, 0.06-1.34) mEq/L.

The number of adults 75 years and older is growing rapidly and is expected to be 10% of the US population by 2030.¹² These older patients characteristically have multiple disease states (diabetes mellitus, CKD, and heart failure) and take an average of more than 5 medications per day.¹³ These patients typically have long-standing hypertension, reduced eGFRs, and/or heart failure, which puts them at increased risk for medication- and disease state-associated changes in potassium homeostasis. Numerous landmark trials demonstrate that use of an RAAS inhibitor provides a significant renoprotective benefit in trials evaluating the use of these agents on CKD progression.¹⁴⁻¹⁶ These results combined with results of other landmark trials have led to the inclusion of RAAS inhibitor therapy in American and European guidelines to treat diabetic kidney disease.¹⁴ However, these benefits come with the risk for hyperkalemia.^{17,18}

In a post hoc analysis of Reduction of Endpoints in NIDDM with the Angiotensin II Antagonist Losartan (RENAAL),¹⁹ it was found that treatment with the ARB

losartan was associated with high risk for hyperkalemia in patients with CKD and diabetic nephropathy. This elevated serum potassium level was associated with increased risk for negative kidney outcomes, which could potentially offset the renoprotective effects of losartan.¹⁹ Currently, patients with CKD and diabetic nephropathy who develop hyperkalemia are advised to reduce their dose of ACE inhibitor or ARB by 50% and reassess serum potassium levels every 5 to 7 days. Although this strategy may alleviate the consequence of hyperkalemia, it also places the patient at increased risk for progression of disease. A recent retrospective analysis of claims data showed that for most patients, physicians do not restart or uptitrate after an episode of hyperkalemia has been resolved.^{2,7} Our data from this current post hoc subgroup analysis of the AMETHYST-DN trial observed 90% of patients entering the long-term maintenance period receiving losartan, 100 mg/d, and receiving patiomer were successfully maintained in the normal serum potassium level range (3.8-5.0 mEq/L) through 52 weeks.

Limitations of the AMETHYST-DN trial have been described elsewhere.¹¹ In short, this is a post hoc subgroup analysis that was not prespecified and had a limited number of patients older than 75 years. As is typical in a small post hoc analysis such as this, no formal examination of power has been undertaken. The open-label design may have affected data reporting through observer bias. Also, there was a lack of a comparator, raising the possibility of regression to the mean, and drug dosing information was not available for all cohorts. Finally, the protocol required that changes in RAAS inhibitor medications were only allowed for the management of blood pressure, so inferences related to changes in RAAS inhibitor use or doses in context to the treatment of hyperkalemia should not be made.

The availability of an effective and well-tolerated potassium binder may be advantageous for an older adult population with multiple disease states.¹⁸ Such an agent may enable more patients with hypertension, advanced kidney disease, and/or heart failure, regardless of cause, the opportunity to initiate and maintain a guideline-recommended RAAS inhibitor dose over long periods.²⁰ Currently there are 2 well-tolerated potassium binders available, patiomer for oral suspension and sodium zirconium cyclosilicate.²¹

As shown in this analysis, the discontinuation of long-term treatment with a potassium binder, in this case patiomer, may lead to a recurrence of hyperkalemia and potentially an associated clinical and economic burden on the health care system.^{7,11,22}

Among older patients with hyperkalemia and diabetic kidney disease, treatment with patiomer reduced serum potassium levels at 4 weeks and maintained normokalemia in most patients 75 years and older through 52 weeks. Patiomer was well tolerated with low rates of discontinuations. The long-term administration of patiomer in older patients with hyperkalemia appears to be effective, be generally safe, and allows the continuation of guideline-

directed medical therapy, consistent with findings in the overall AMETHYST-DN population.¹¹

SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

Figure S1. Patient disposition.

ARTICLE INFORMATION

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Support: The analysis reported in this manuscript and medical writing assistance and editorial support were funded by Vifor Pharma, Inc. The sponsor had a role in the study design, conduct of the study, data collection, data, interpretation, and decision to publish. The findings and conclusions in this article are those of the authors, who are responsible for its contents.

Financial Disclosure: Dr Bakris reports employment by the University of Chicago; consultant fees from AstraZeneca, Janssen, Merck, NovoNordisk, and Vifor Pharma, Inc.; and research support paid to the University of Chicago by Bayer, Janssen, and Vascular Dynamics. Dr Woods, Ms Alvarez, and Dr Arthur report employment by and stock in Vifor Pharma, Inc. Dr Kumar has no relevant relationships to report.

Acknowledgements: Editorial support services were provided by Impact Communication Partners, Inc.

Prior Presentation: These results were presented at the American Diabetes Association 79th Scientific Sessions, San Francisco, CA, June 7-11, 2019; the 14th Annual Cardiometabolic Health Congress, Chicago, IL, October 10-13, 2019; and the American Society of Consultant Pharmacists 2019 Annual Meeting & Exhibition, Grapevine, TX, November 7-10, 2019.

Peer Review: Received October 8, 2020, as a submission to the expedited consideration track with 3 external peer reviews. Direct editorial input from the Statistical Editor and the Editor-in-Chief. Accepted in revised form January 17, 2021.

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Is patiromer safe and effective in lowering serum potassium among elderly CKD patients receiving RAAS inhibitors?



Methods and Cohort

Multicenter, open-label RCT

AMETHYST-DN
≥75 years old
(N = 60)

Patiromer
8.4–33.6 g TDD

Post hoc Subgroup Analysis

52 weeks

Patient Disposition

77
Mean Age

50%
Men

42
mL/min/1.73m²
Mean eGFR

5.2
mEq/L
Mean serum K

40
Completed study

Findings

Least squares-mean reduction of serum K⁺

-0.65 mEq/L Week 4 -0.61 mEq/L Week 52

Serum K⁺ at the end of 52 weeks

100% of patients had Serum K <5.5 95% of patients had Serum K <5.0

Serum K⁺ after stopping patiromer

4.79 mEq/L after 3 days
4.85 mEq/L after 7 days
4.95 mEq/L after 14 days

Adverse Effects

10 patients with at least 1 patiromer-related AE
0 cases of hypokalemia or severe hypomagnesemia

Most common AE leading to drug discontinuation
GI symptoms (2), Chronic kidney failure (2)

Conclusion: Among older patients with hyperkalemia and diabetic kidney disease, treatment with patiromer resulted in significant reductions in serum potassium levels after 4 weeks and lasted through 52 weeks. Patiromer was effective in lowering serum potassium and was well tolerated in older patients.

Reference: Bakris GL, Woods SD, Alvarez PJ, et al. Hyperkalemia management in older adults with diabetic kidney disease receiving renin-angiotensin-aldosterone system inhibitors: a post hoc analysis of the AMETHYST-DN clinical trial. *Kidney Medicine*, 2021.

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